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Investor Day
October 3, 2022

Envisioning a new way to treat cancer

Legal Disclosure

This presentation contains forward-looking statements, all of which are qualified in their entirety by this cautionary statement. Many of the forward-looking statements contained herein can be identified by the use of forward-looking words such as "may", "anticipate", "believe", "could', "expect", "should", "plan", "intend", "estimate", "will", "potential" and "ongoing", among others, although not all forward-looking statements contain these identifying words. These forward-looking statements include statements about the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs; our ability to successfully manufacture our drug substances and product candidates for preclinical use, for clinical trials and on a larger scale for commercial use, if approved; the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and product candidates; our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates; our ability to obtain and maintain regulatory approval of our product candidates; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; our financial performance; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials; our ability to commercialize our products, if approved; and the implementation of our business model, and strategic plans for our business and product candidates.

Except as otherwise noted, these forward-looking statements speak only as of the date of this presentation, and we undertake no obligation to update or revise any of such statements to reflect events or circumstances occurring after this presentation. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We caution you not to place undue reliance on the forward-looking statements contained in this presentation.

This presentation discusses product candidates that are under preclinical or clinical evaluation and that have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory authority. Until finalized in a clinical study report, clinical trial data presented herein remain subject to adjustment as a result of clinical site audits and other review processes. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

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Agenda

Welcome and Introduction	*Elisabet de los Pinos, PhD* *Cadmus Rich, MD*
Preclinical Data on Choroidal Metastasis and Belzupacap Sarotalocan in Combination With Immune Checkpoint Inhibition	*Martine Jager, MD, PhD*
Two-Year Retrospective Matched Case Control	*Carol Shields, MD*
Phase 2 Suprachoroidal Safety and Efficacy	*Ivana Kim, MD, MBA*
Moderated Q&A with Ocular Oncology Thought Leaders	*Cadmus Rich, MD (moderator)*
Audience Q&A	*Elisabet de los Pinos, PhD (moderator)*
Conclusion and Closing Remarks	*Elisabet de los Pinos, PhD*

Novel Oncology Platform Using Virus-Like Drug Conjugates (VDCs)

Ocular Oncology Franchise

- Multi-billion dollar market opportunity
- Standard of care is invasive and may lead to blindness and eye loss

Foundational Value

- Completed Phase 1b/2 trial: Positive data in key clinical endpoints
- FDA/EMA/MHRA are in alignment with pivotal trial design

Oncology Pipeline

- Solid tumor development programs
- Platform to develop additional VDCs

Clinical & Regulatory Milestones

- Ocular Oncology Franchise
  - ✓ Retrospective vision data versus radiotherapy
  - ✓ Phase 2 Choroidal Melanoma safety and efficacy data
  - Initiate Pivotal Trial in Choroidal Melanoma
  - IND filing in Choroidal Metastasis
- Oncology Franchise
  - ✓ Initiate Phase 1 in Non-Muscle Invasive Bladder Cancer

Strong Investor Base

- Strong Cash Position

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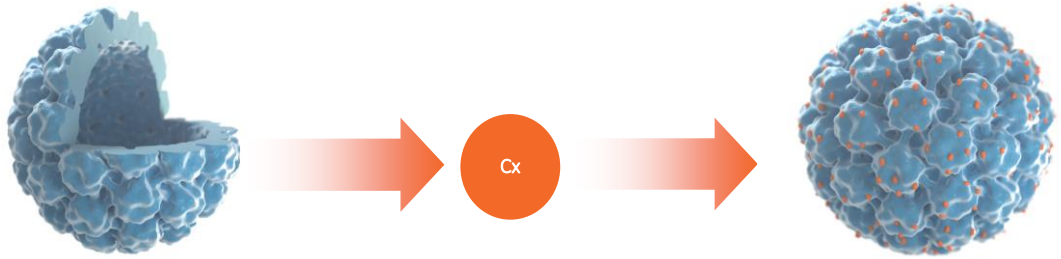
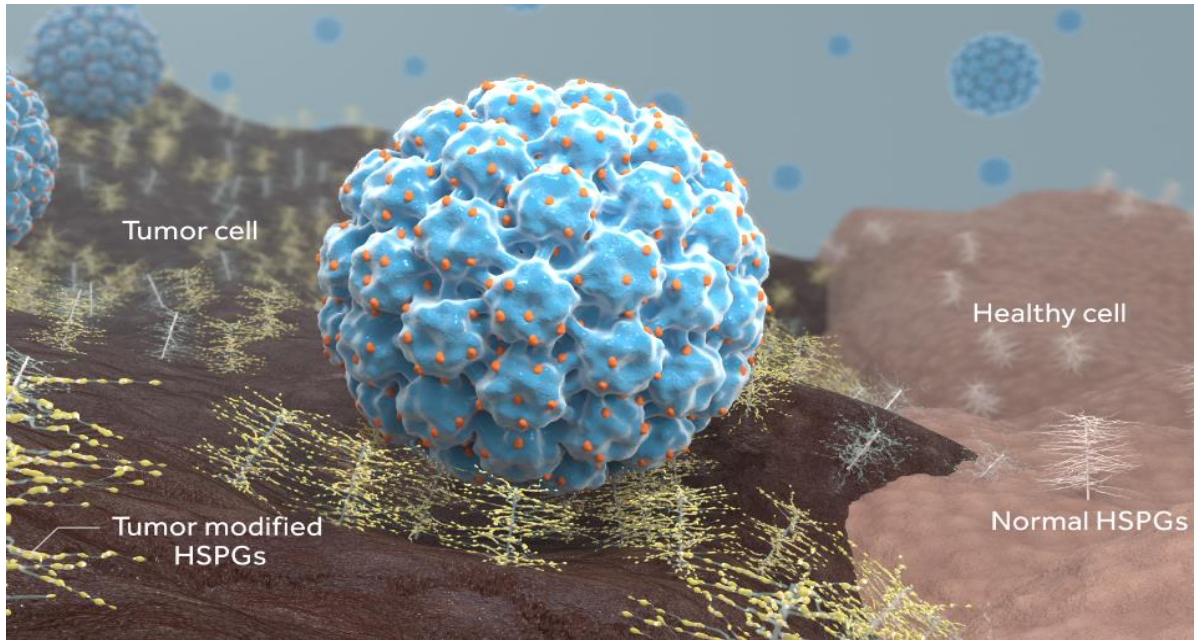
Targeted Oncology Platform - Virus-Like Drug Conjugates (VDCs)

Virus-Like Particles Conjugated to a Cytotoxic Payload to form the VDC



Virus-Like Particle (VLP) | Cytotoxic Drug | Virus-Like Drug Conjugate (VDC)

VDCs can Recognize Tumor Associated HSPGs*



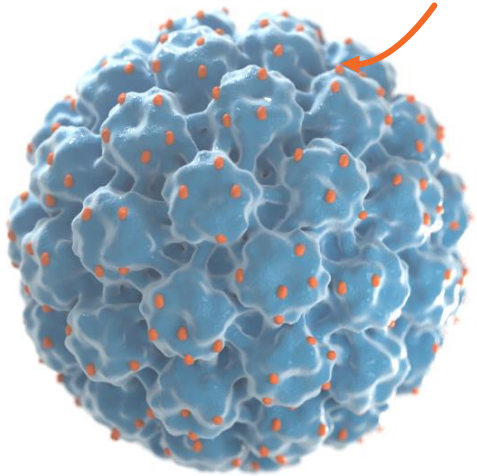
Technology Platform Designed to Target a Broad Range of Solid Tumors Based on Virus-Like Particles with Multiple Options for Cytotoxic Payloads

Kines et al; *International Journal of Cancer*, 138;901–911, February 2016; Kines et al; *Molecular Cancer Therapeutics*, 17(2) February 2018; Kines et al; *Cancer Immunology Research*, May 2021

* HSPGs: Heparan Sulphate Proteoglycans

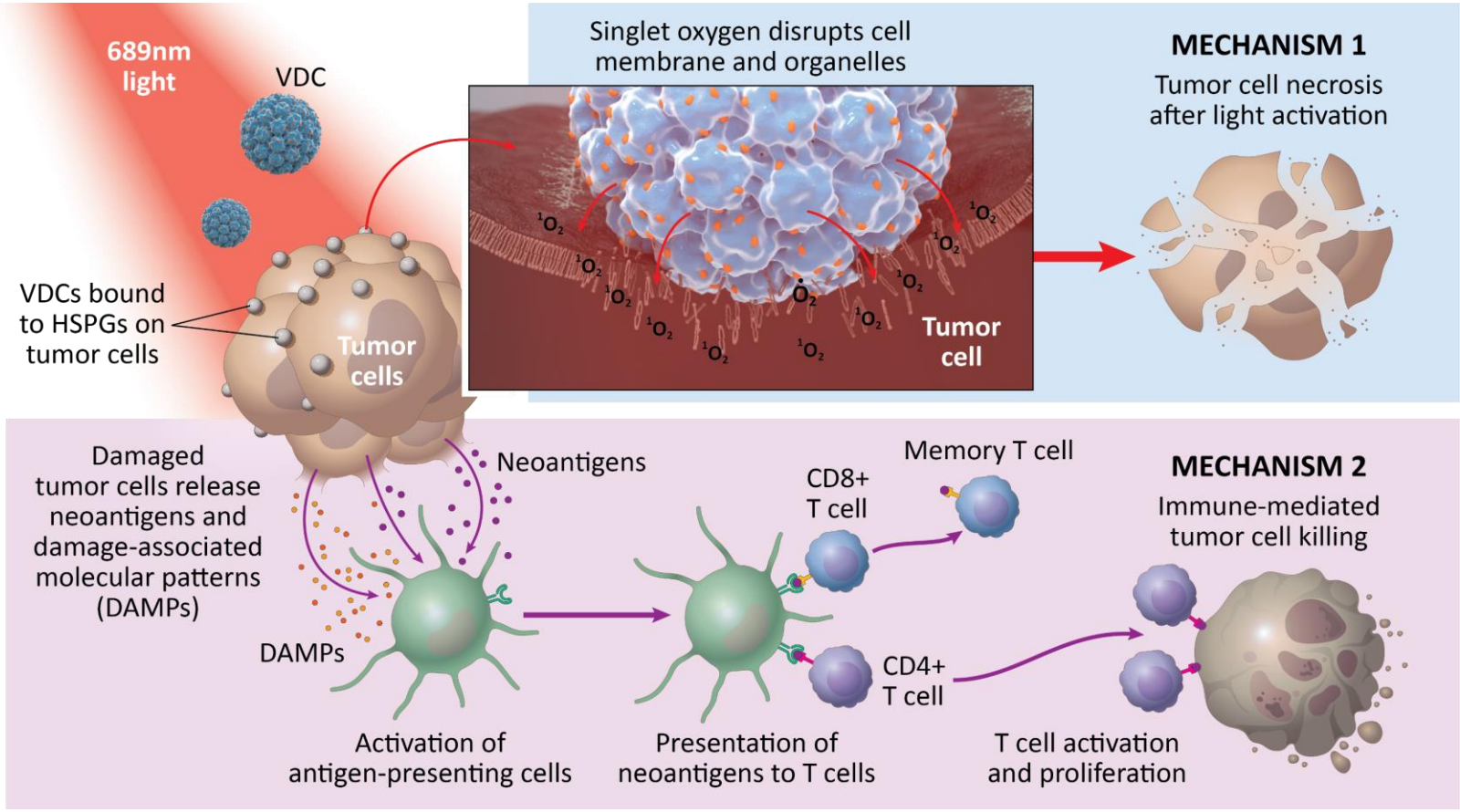
Belzupacap sarotalocan (AU-011) is a VDC with a Novel Dual Mechanism of Action

Light Activated Drug



Belzupacap Sarotalocan

Belzupacap Sarotalocan is a novel VDC that consists of a VLP conjugated to ~200 molecules of phthalocyanine dye



Potential Key Differentiation: Physical Ablation may Reduce Risk to Develop Resistance and is Genetic Mutation Agnostic

Kines et al; Cancer Immunology Research, May 2021

We are pleased to welcome…

Ocular Oncology Thought Leaders

Martine Jager, MD, PhD

Professor of Ophthalmology, Leiden University, (Netherlands) & Past President of the International Society of Ocular Oncology and the Association for Research in Vision and Ophthalmology

Universiteit Leiden

Carol Shields, MD

Chief of the Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University (Philadelphia, PA)

WillsEye Hospital

Jefferson
Thomas Jefferson University
HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

Ivana Kim, MD, MBA

Director of the Ocular Melanoma Center, Massachusetts Eye and Ear & Associate Professor of Ophthalmology, Harvard Medical School (USA)

MASSACHUSETTS EYE AND EAR

HARVARD MEDICAL SCHOOL | DEPARTMENT OF Ophthalmology

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Preclinical Research and Collaborative Work with Leiden University

Leids Universitair Medisch Centrum

Preclinical Data on Choroidal Metastasis and Belzupacap Sarotalocan in Combination With Immune Checkpoint Inhibition

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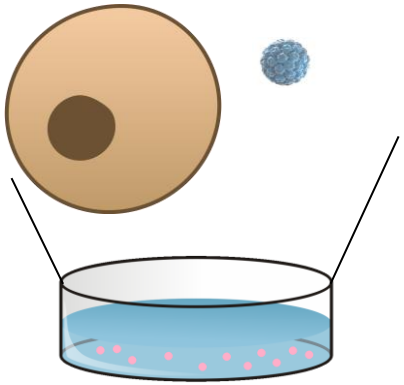
Research sponsored by Health Holland
in collaboration with Aura Biosciences

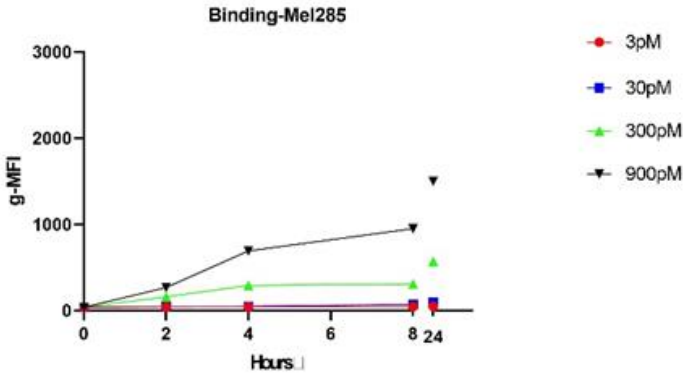
Health~ Holland

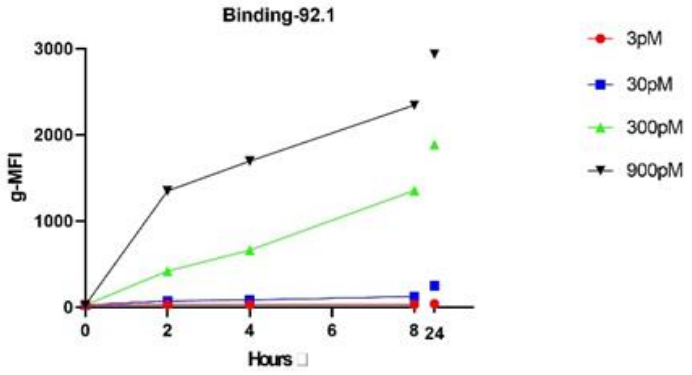
Martine Jager, MD, PhD

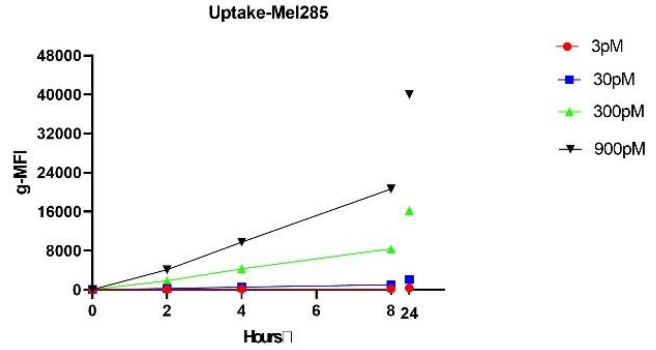
AU-011 has shown binding and uptake in uveal melanoma cells

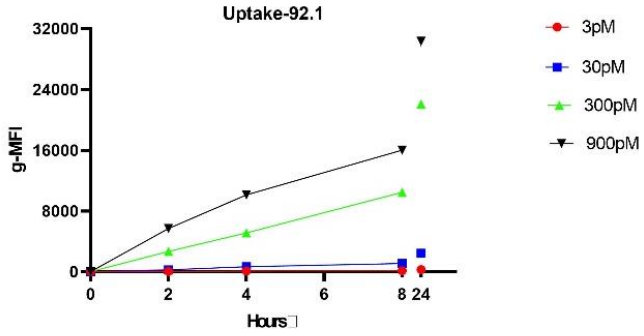
Cancer cells AU-011





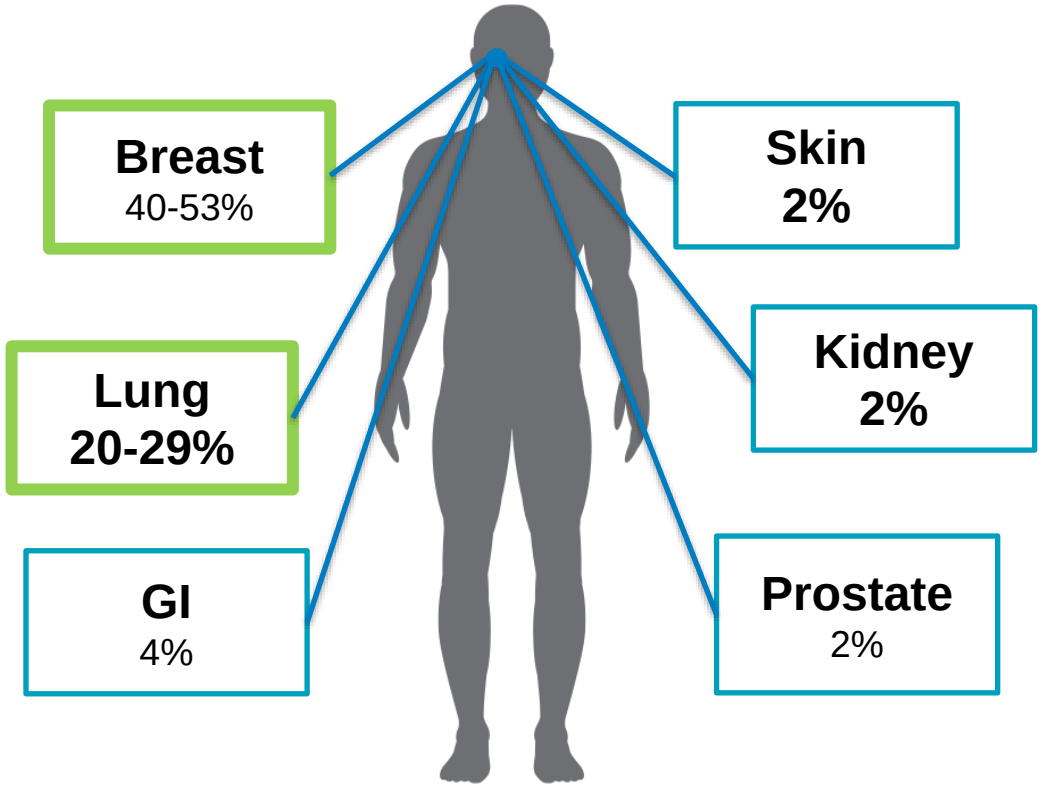






Belzupacap Sarotalocan Potential Applicability in Other Ocular Cancers is Being Investigated - Choroidal Metastasis

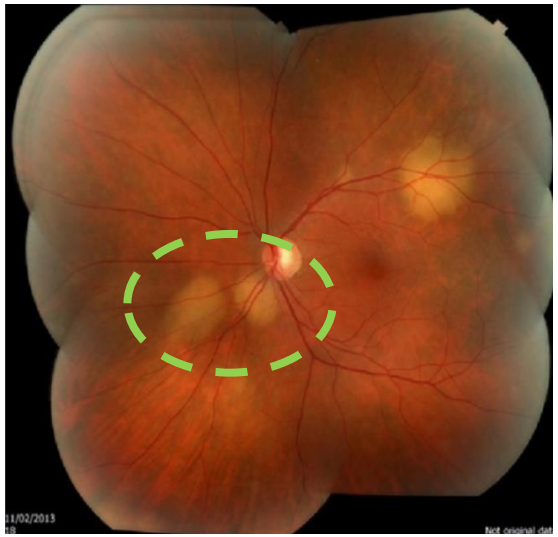
C-Mets Originates from Multiple Primary Cancers[1]



~20K eyes with choroidal metastases in the U.S. annually[2]

Common Features of C-Mets[3]

- Unilateral (72%)
- Solitary (72%)
- Choroidal location (88%)

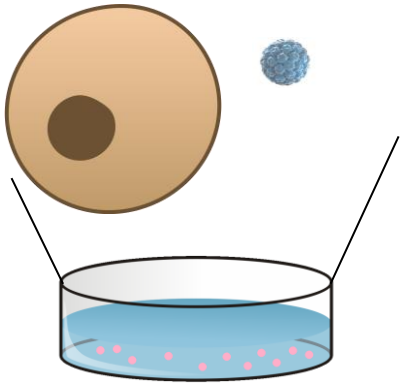


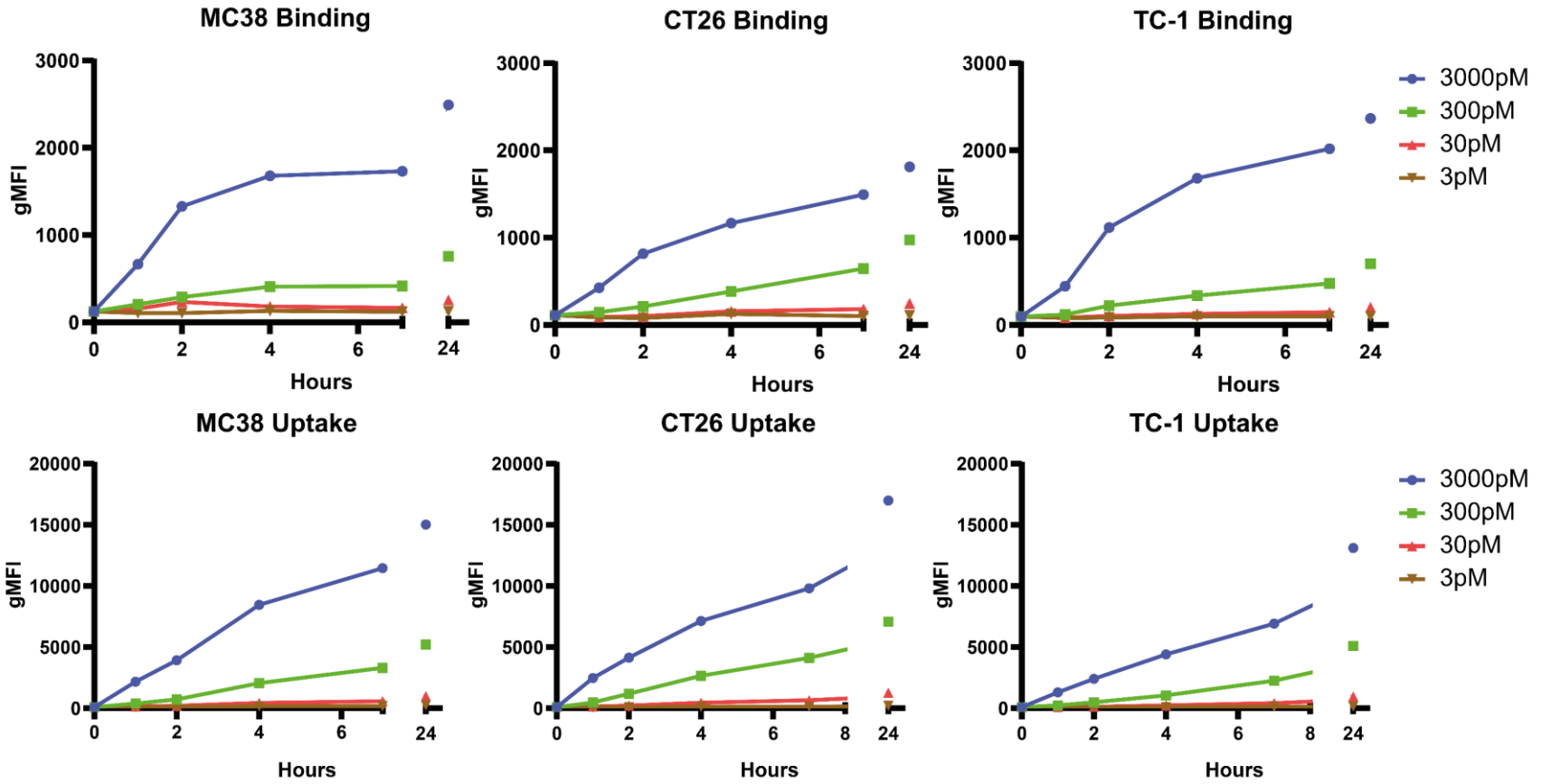
Choroidal Metastasis from non-small cell lung cancer[4]

[1]Mathis et al. New concepts…choroidal metastasis, *Progress in retinal and eye research* (2019), [2]Cohen, Ocular metastasis, Eye (2014), [3]Shields et al. Survey of 520 eyes with uveal metastases. *Ophthalmology* (1997), [4]Namad et al. Bilateral choroidal metastasis from non-small lung cancer, Case reports in oncological medicine (2014).

AU-011 has shown binding and uptake in multiple types of tumor cells

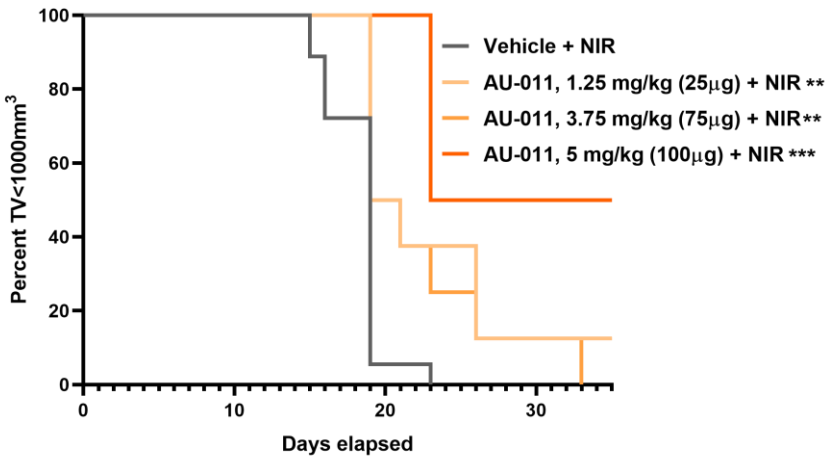
Cancer cells AU-011



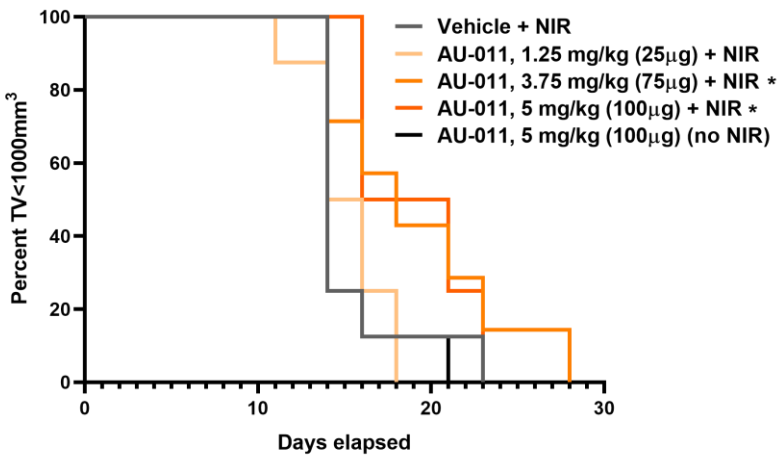


Belzupacap Sarotalocan Has Demonstrated Dose-dependent Activity For Cancer Types Known To Metastasize To The Choroid

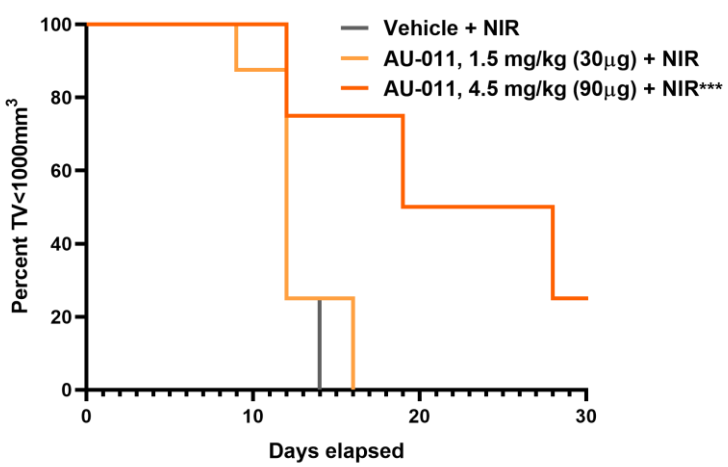
BREAST EMT6



RENAL RENCA



COLON CT26



Single administration of belzupacap sarotalocan inhibited tumor growth and prolonged survival in a dose-dependent fashion

Savinainen et al., ARVO 2022 Abstract # 3709397 NIR = near-infrared light. Endpoint is percent of tumors reaching the threshold volume of 1000mm^3

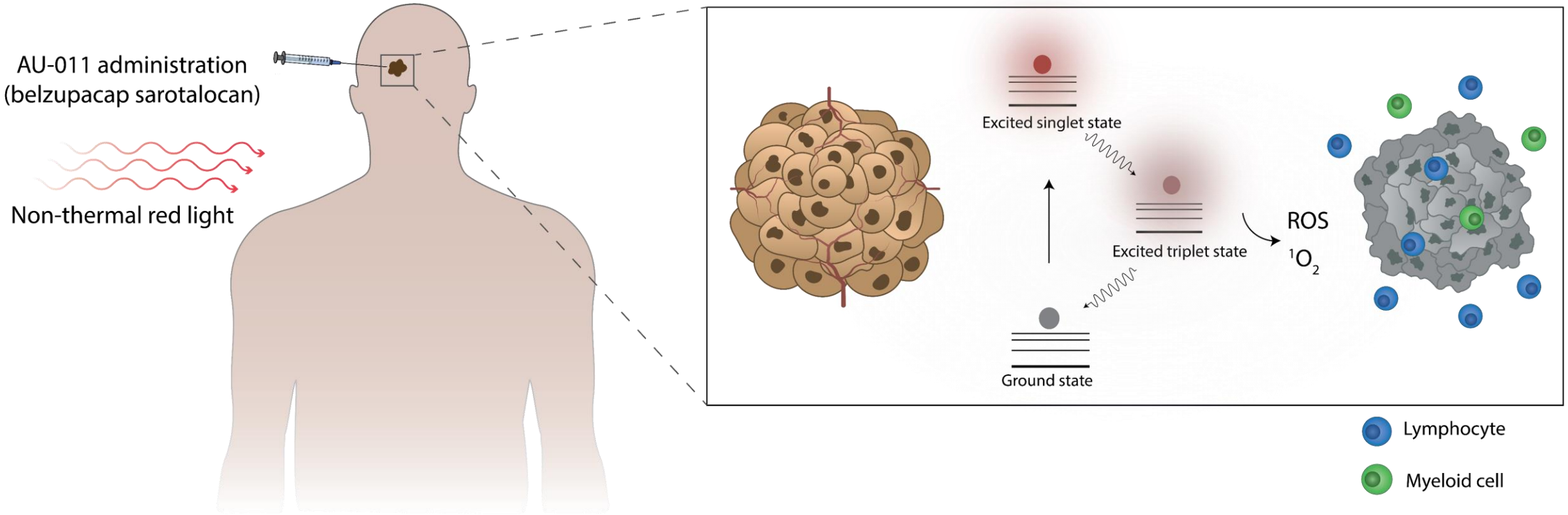
Conclusions – Preclinical Work in Choroidal Metastasis

Belzupacap sarotalocan showed dose-dependent activity in vivo using syngeneic mouse models for cancer types known to metastasize to the choroid

- Significantly inhibits tumor growth and prolongs survival
- Statistically significant results in multiple tumor models

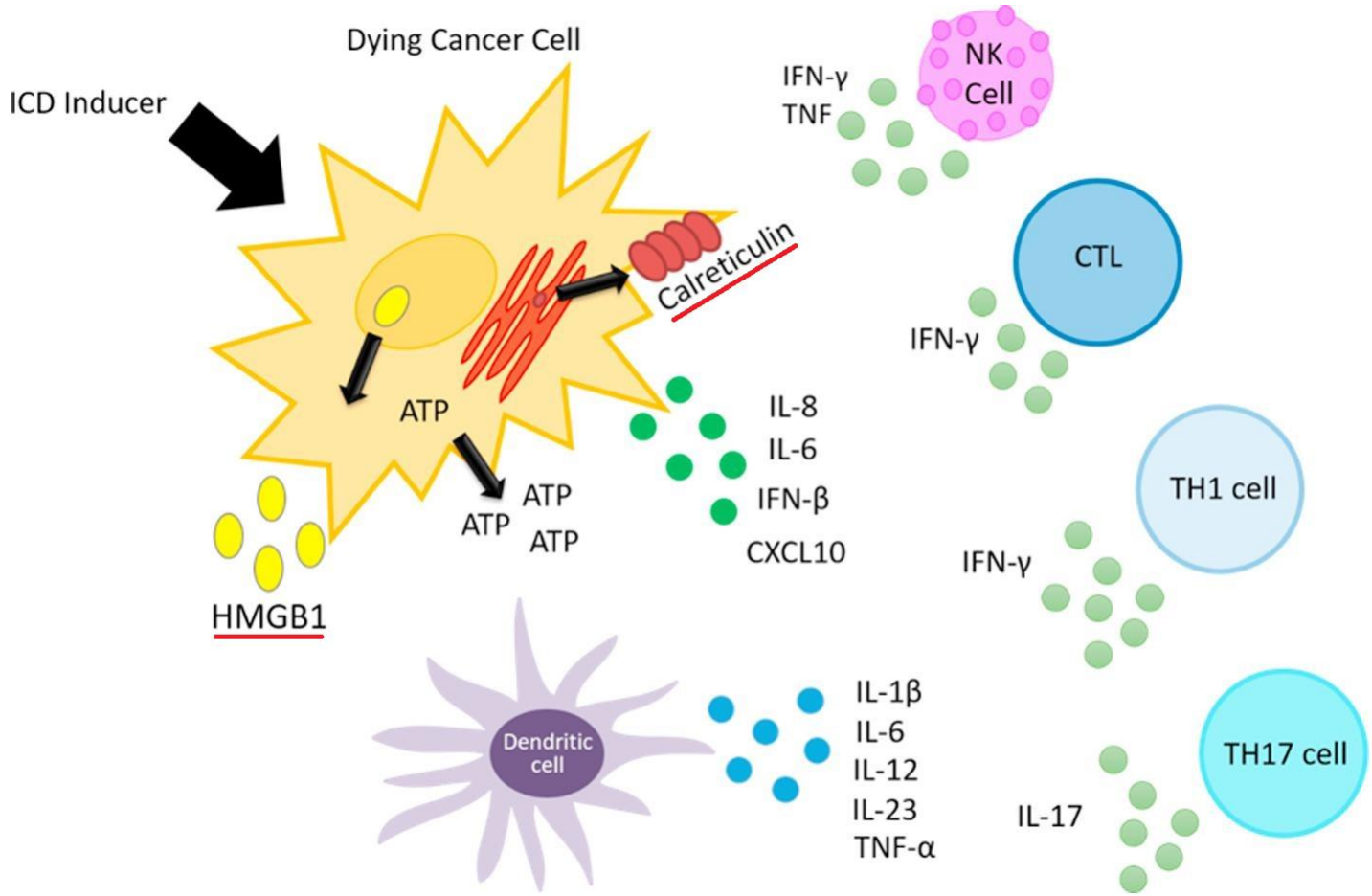
Study results support further evaluation of belzupacap sarotalocan as a potential treatment for ocular cancers, including those that metastasize to the choroid

AU-011 is an investigational virus like drug conjugate with a novel mechanism of action



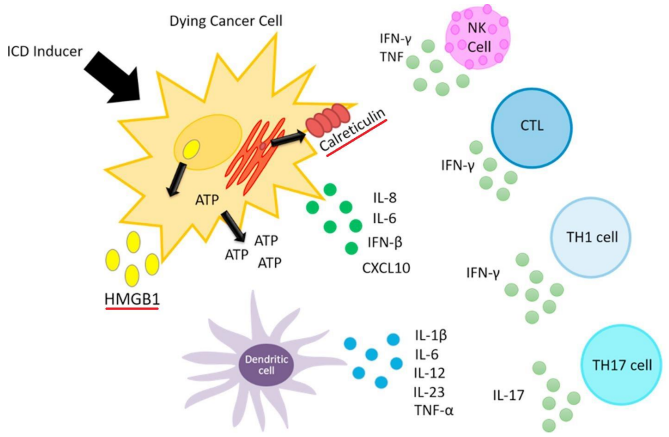
1. Cancer cell directed cytotoxicity
2. Induction of antitumor immune responses

Damage-associated molecular patterns (DAMPs)



Showalter A. et al. Cytokines in immunogenic cell death: Applications for cancer immunotherapy. Cytokine. 2017;97:123-132

Release of DAMPs following AU-011 treatment



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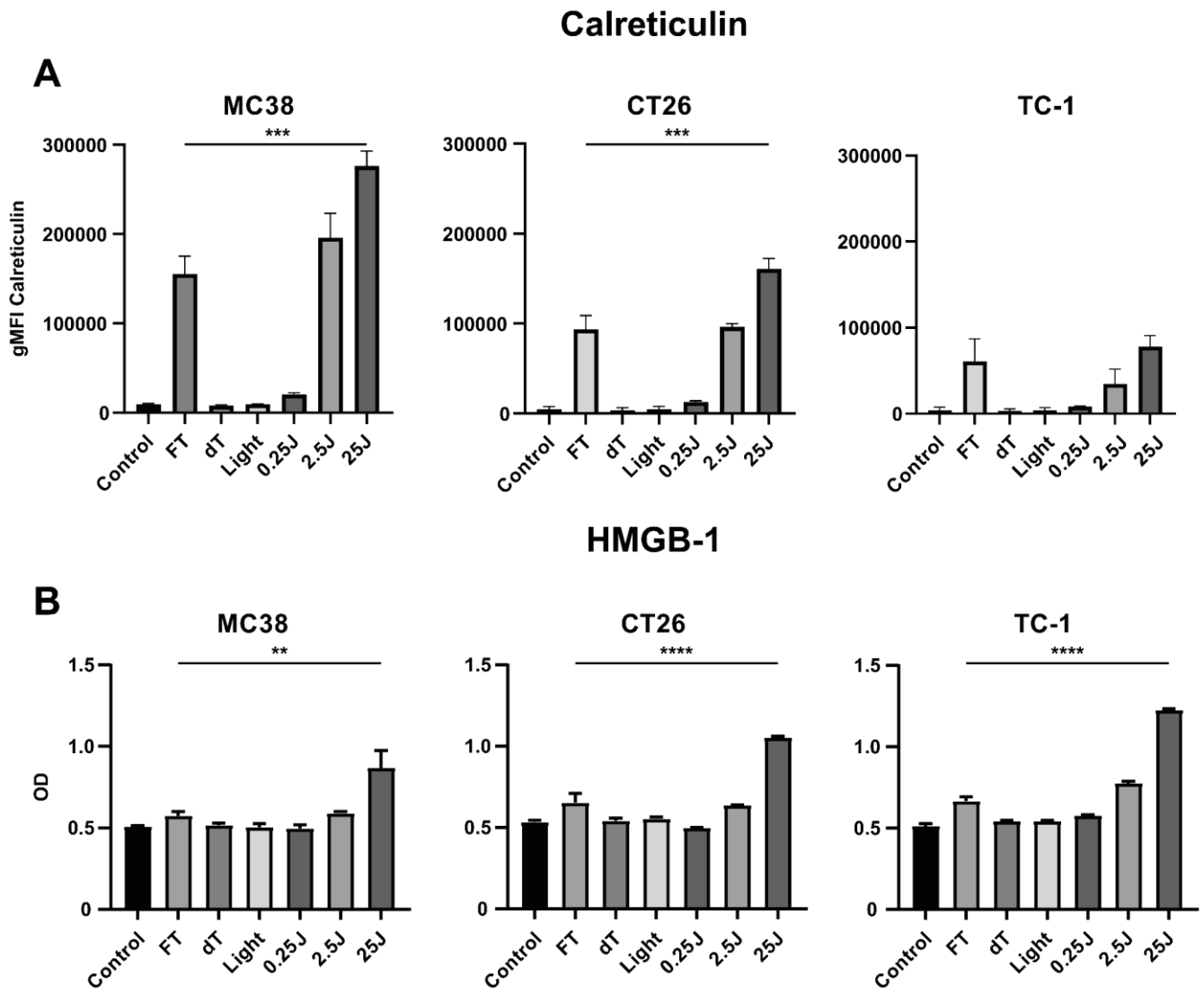
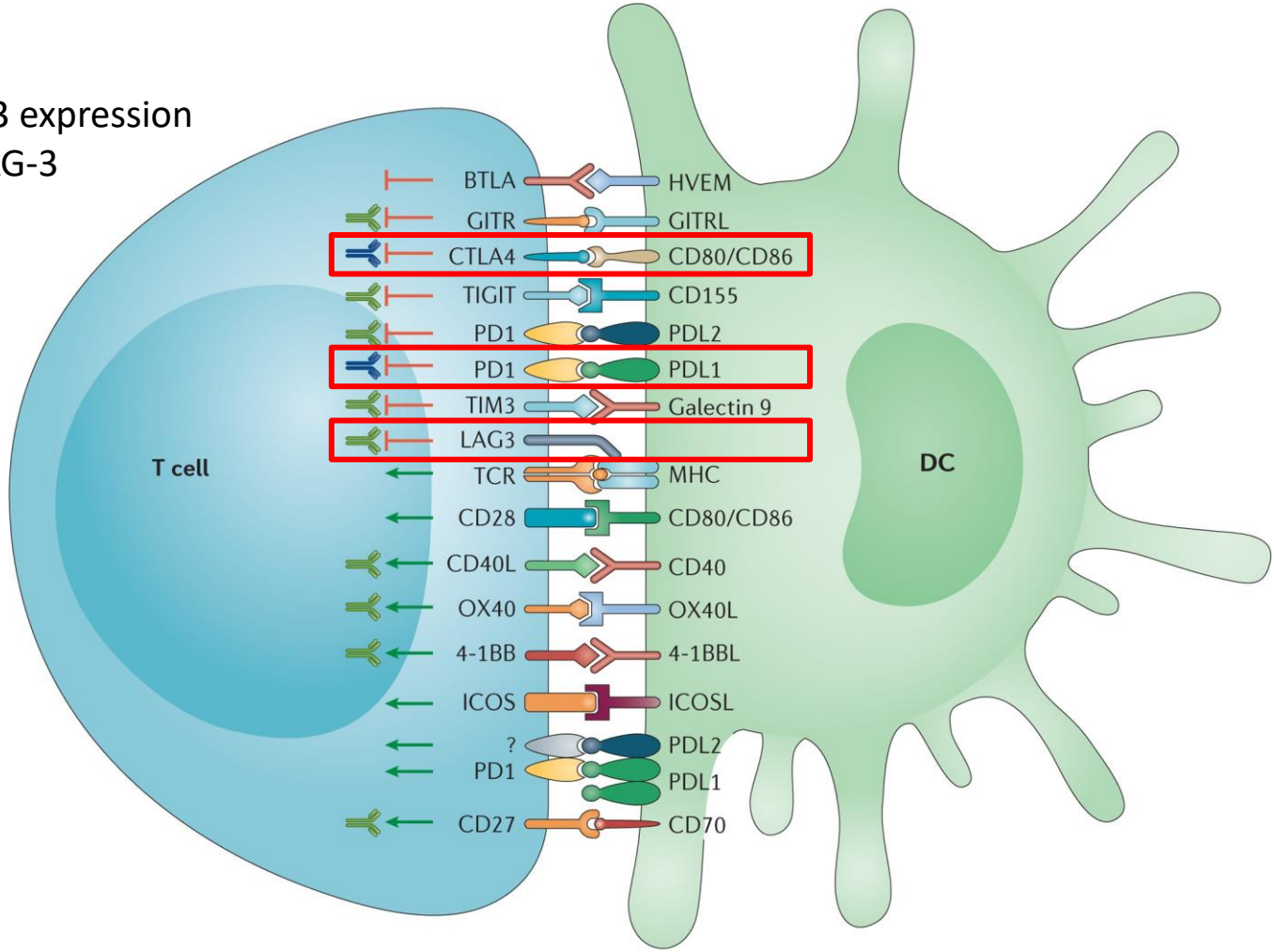


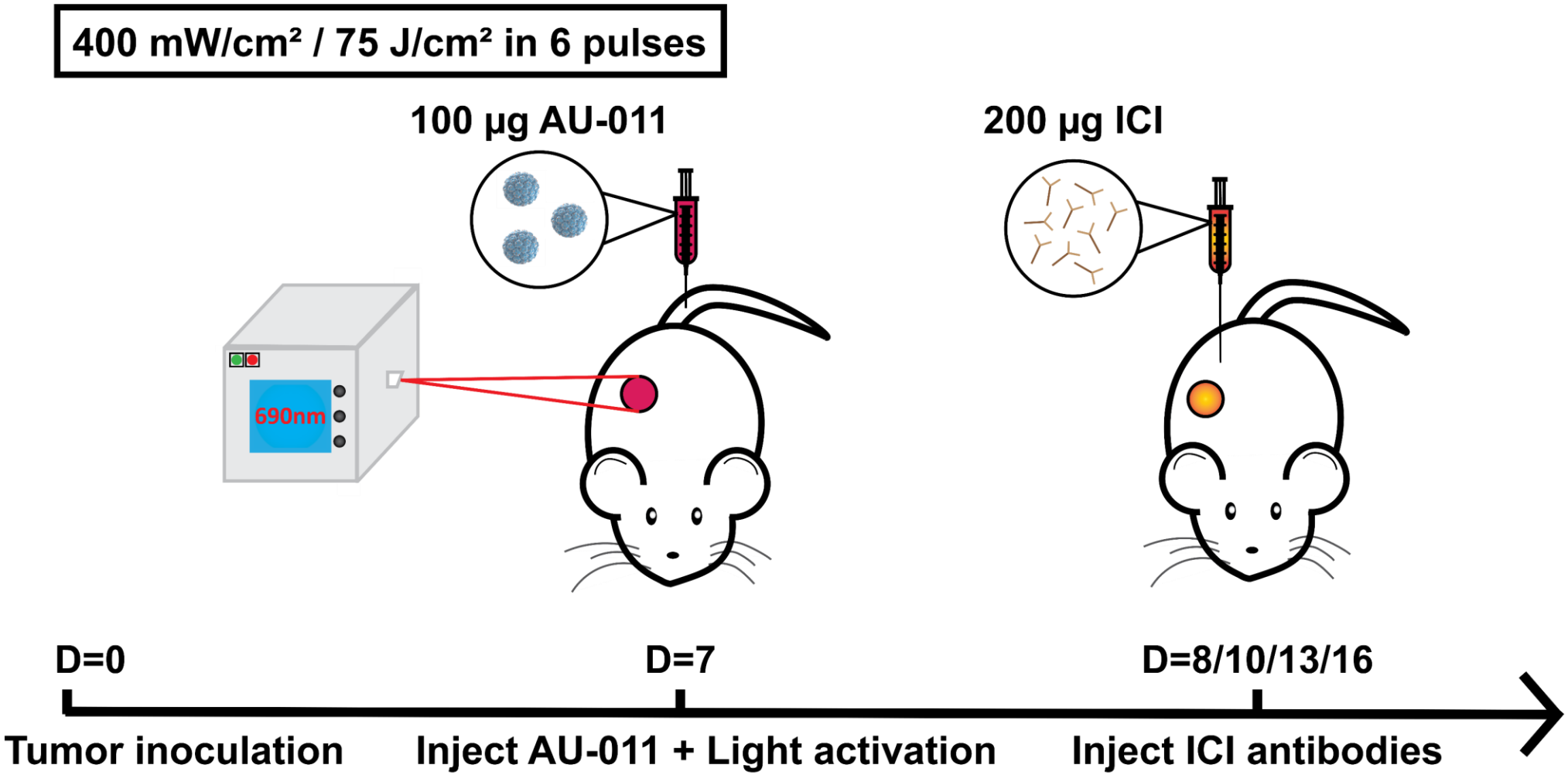
Rationale for combining AU-011 treatment and Immune Checkpoint Inhibition: T cells are inhibited through ICI's

Beyrend et al. (2019):
PD-L1 blockade induces LAG-3 expression
→ Co-targeting of PD-L1 & LAG-3

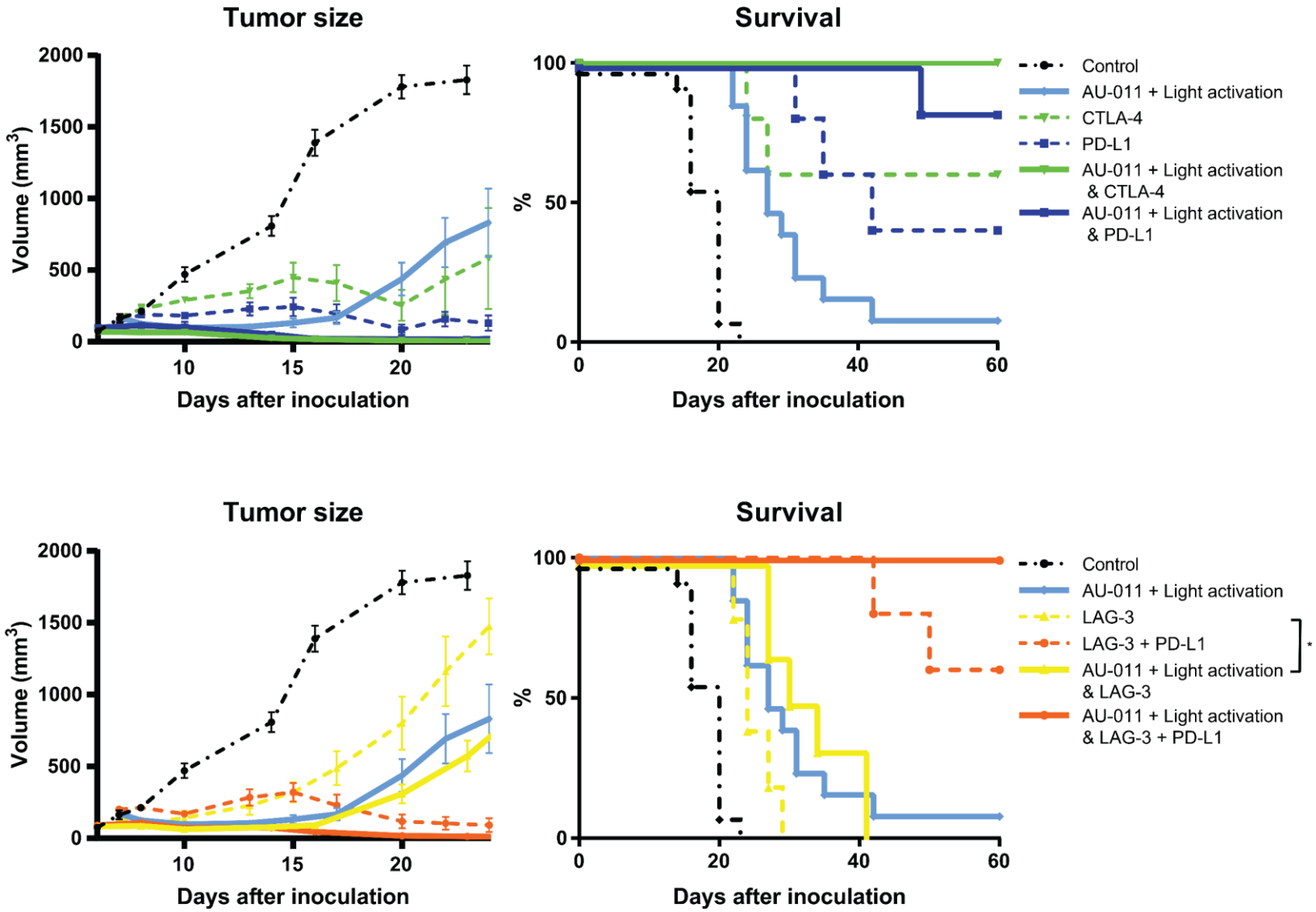


Wykes M. N. & Lewin S. R. Immune checkpoint blockade in infectious diseases. Nature Reviews Immunology. 2018;18:91–104

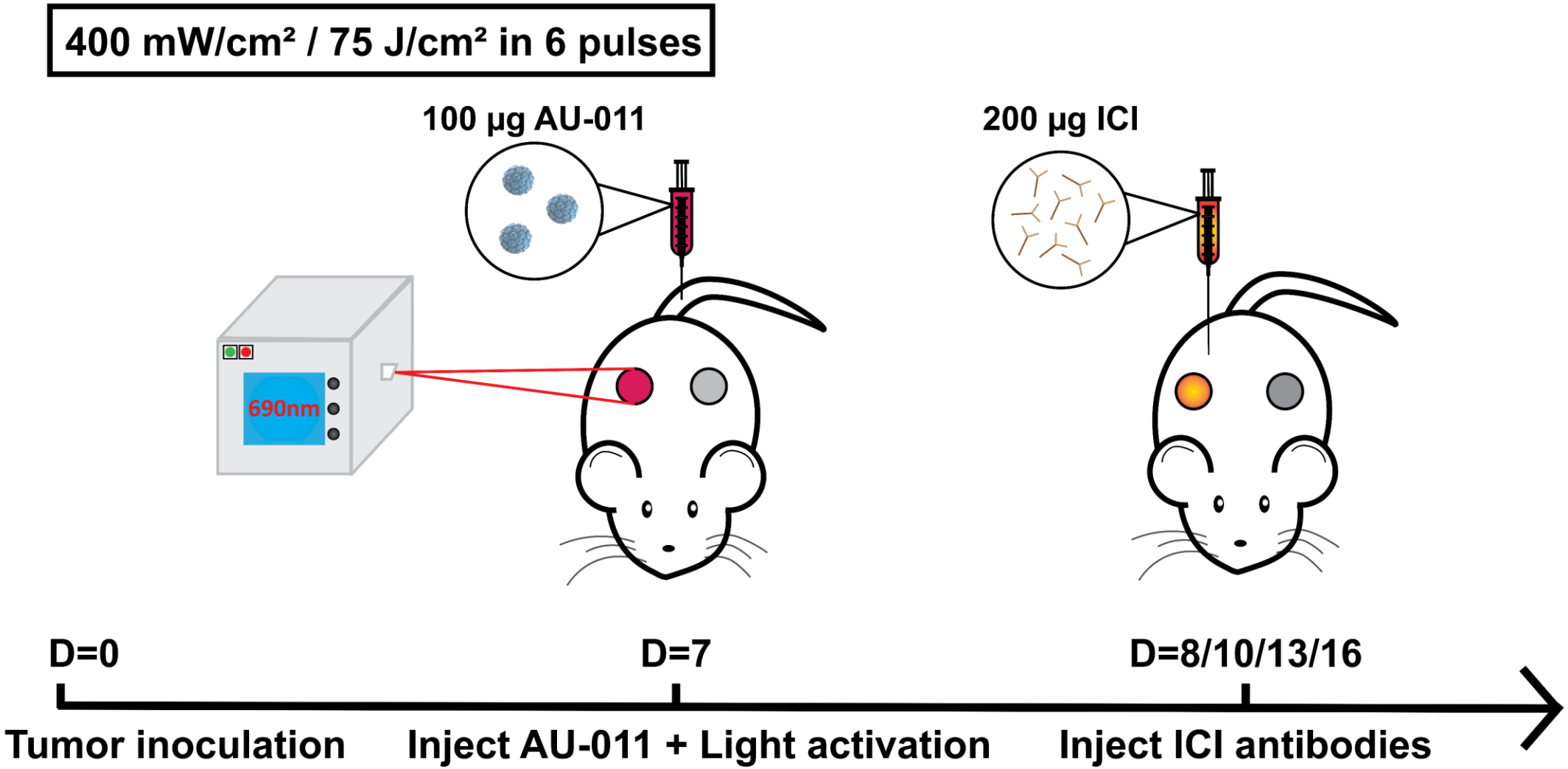
AU-011 + Light activation combined with ICI enhanced treatment response compared to either treatment alone (1 of 2)



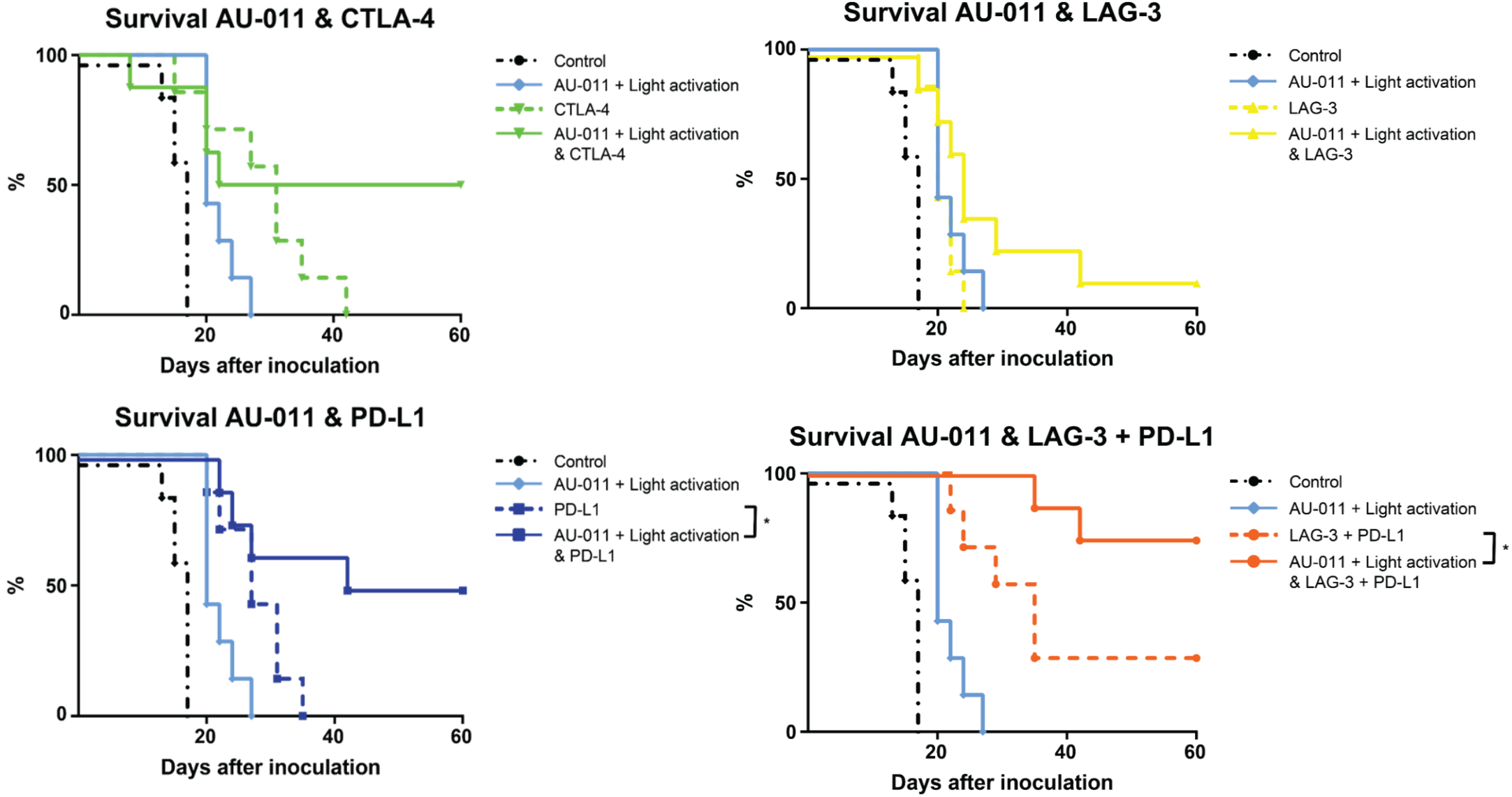
AU-011 + Light activation combined with ICI enhanced treatment response compared to either treatment alone (2 of 2)



Treatment of primary and distant tumors was enhanced by AU-011 + Light activation with ICI versus either treatment alone (1 of 3)



Treatment of primary and distant tumors was enhanced by AU-011 + Light activation with ICI versus either treatment alone (3 of 3)

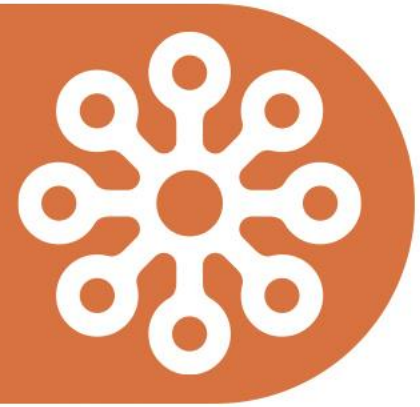


Conclusions – Collaborative Work

AU-011 + Light activation:

- **Induced cancer cell-directed cytotoxicity**
- **Released DAMPs and induced maturation of antigen-presenting cells**
- **Combined with ICI using anti-PD-L1 & anti-LAG-3 antibodies showed potential to induce complete and lasting tumor responses in both primary and distant tumors in murine models**

Two-Year Retrospective Matched Case Control of AU-011 vs Plaque Radiotherapy for Uveal Melanoma: Visual Outcomes



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Timeline of Uveal Melanoma

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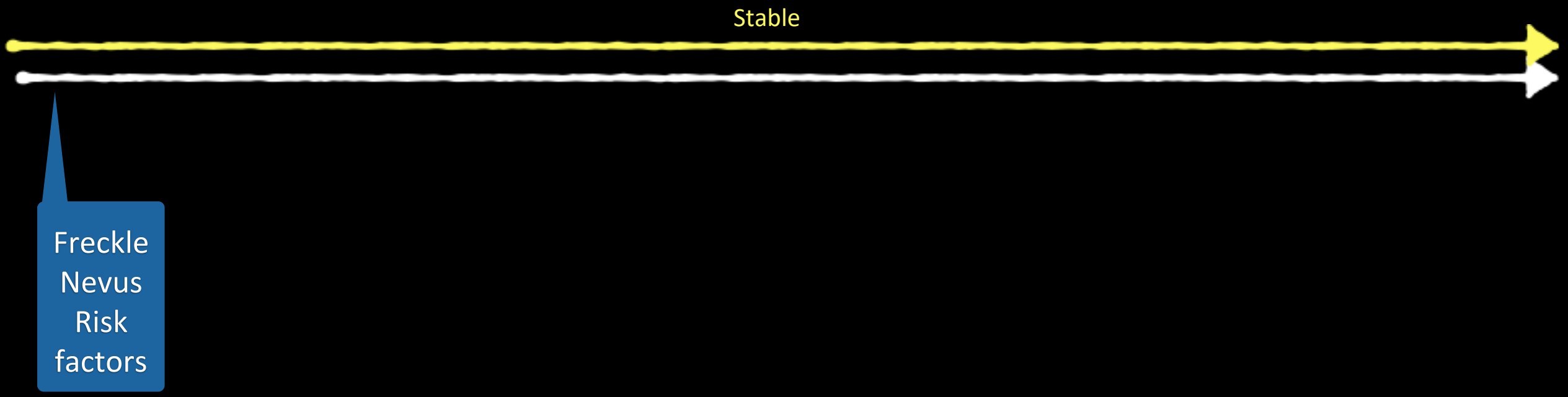

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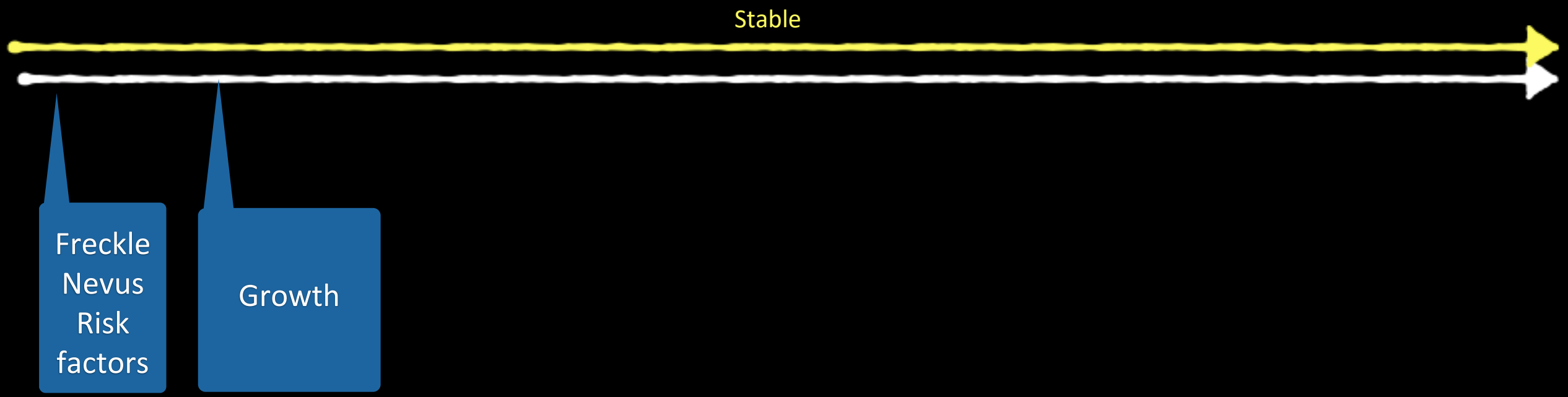
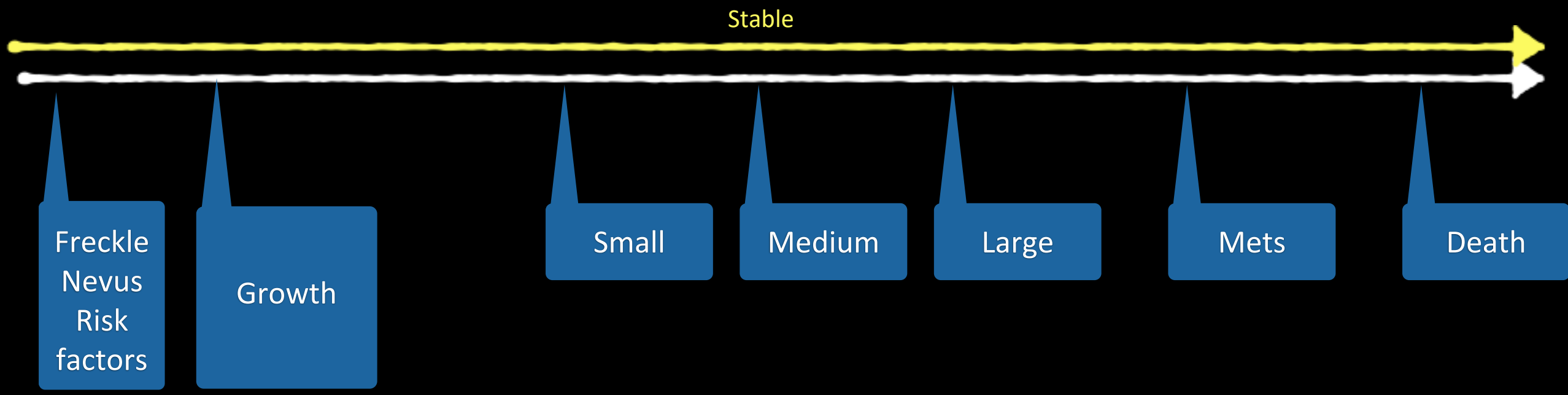
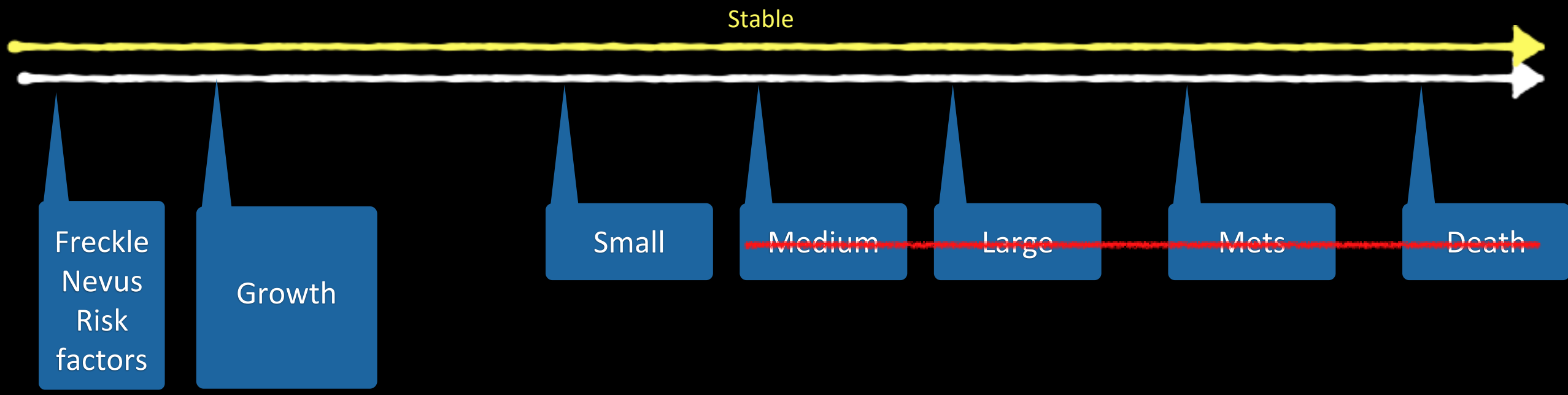


Timeline of Uveal Melanoma



Timeline of Uveal Melanoma



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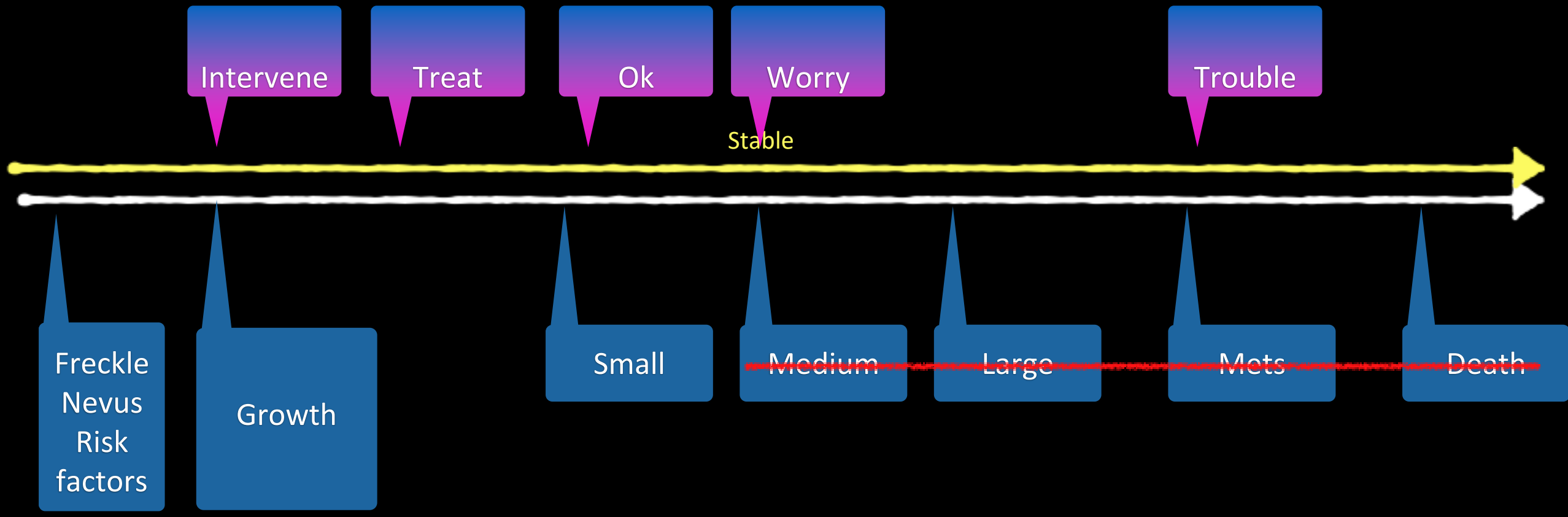

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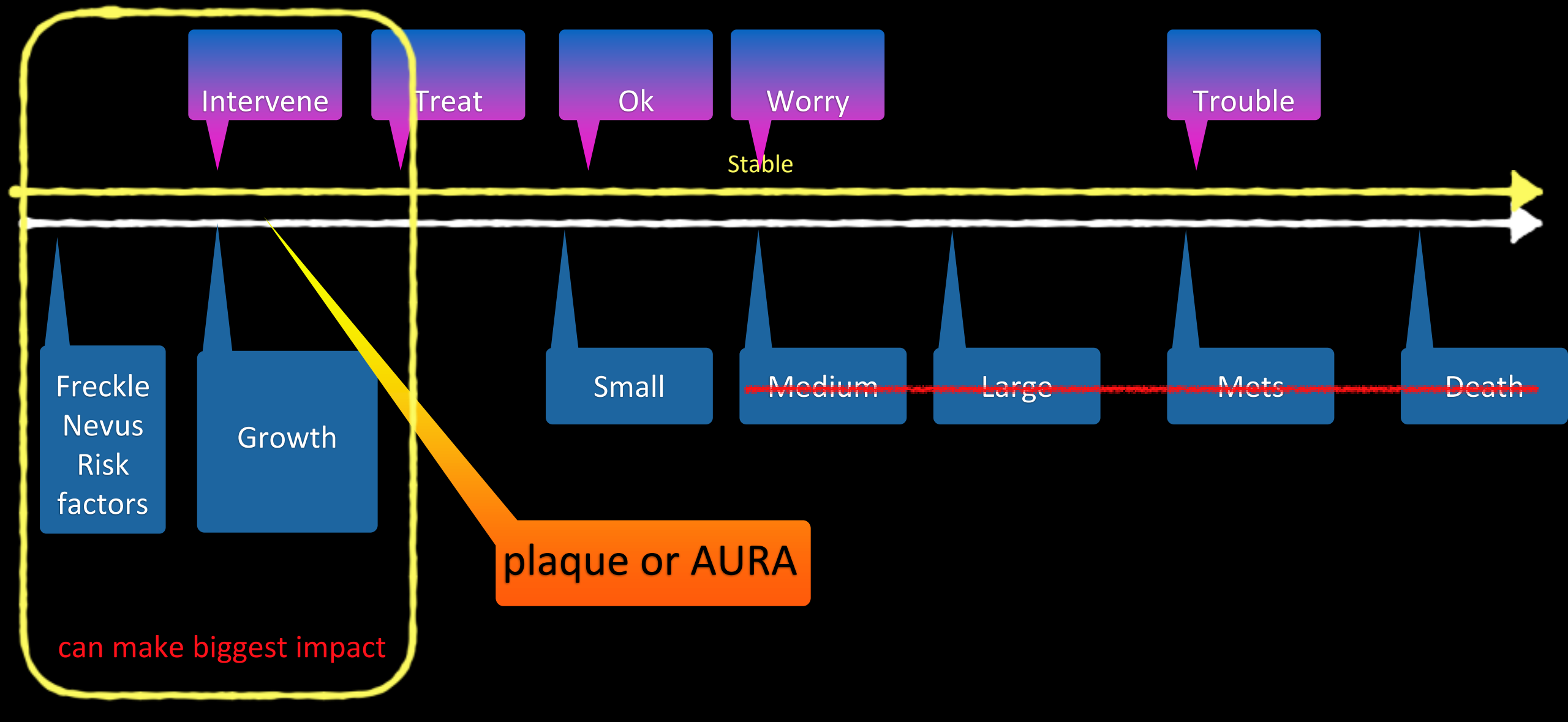
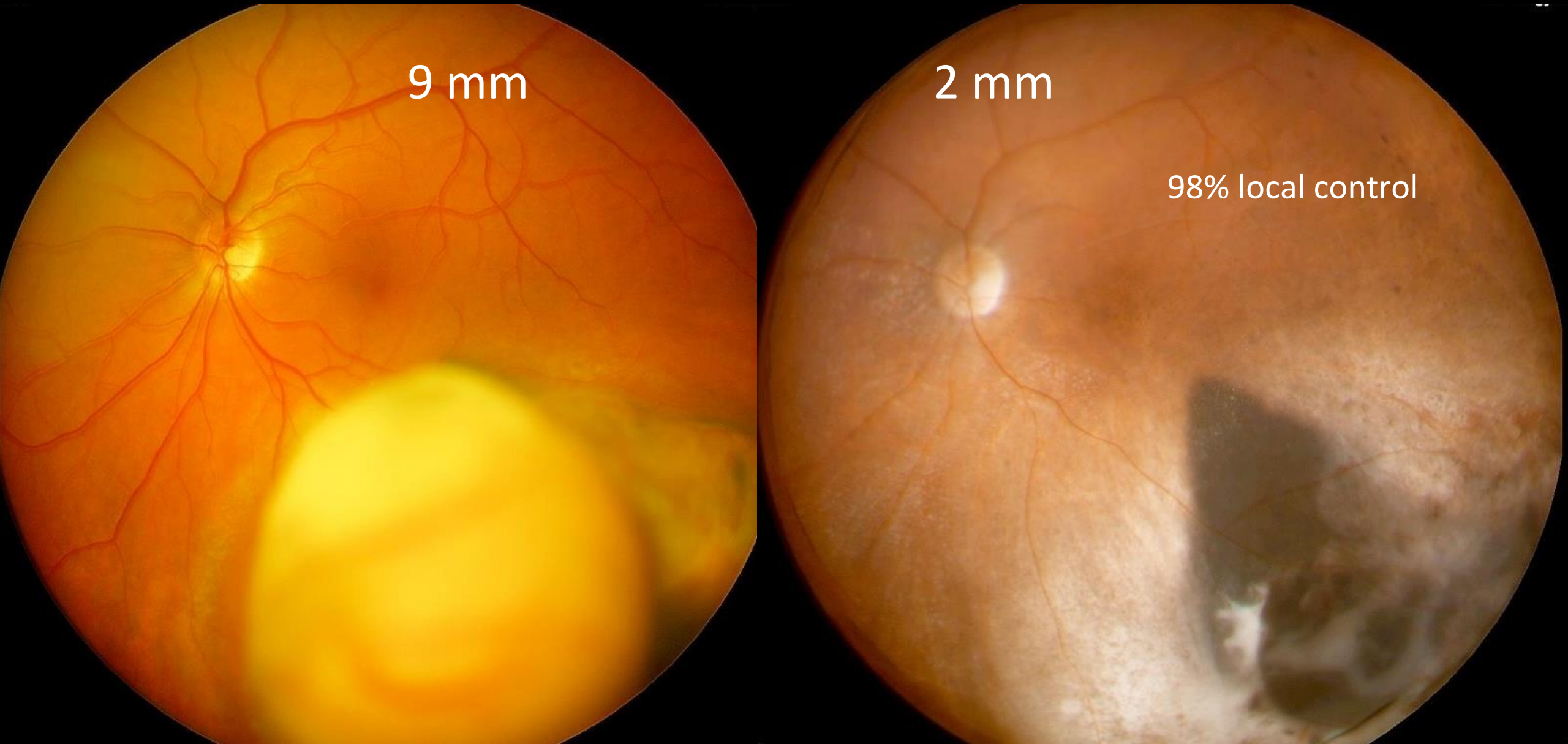


Melanoma Therapy

- Enucleation
- Plaque radiotherapy
- Proton beam radiotherapy
- Stereotactic radiotherapy
- Gamma/cyber knife radiotherapy
- Local resection
- Transpupillary thermotherapy
- AU-011 Nanoparticle therapy

Plaque radiotherapy



Plaque radiotherapy

Complications

Radiation-related

- Retinopathy
- Papillopathy
- Choroidopathy
- Cataract
- Glaucoma
- Scleral necrosis

Plaque radiotherapy

Complications
Radiation-related

… with profound vision loss [blindness], even for small melanoma

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Plaque radiotherapy

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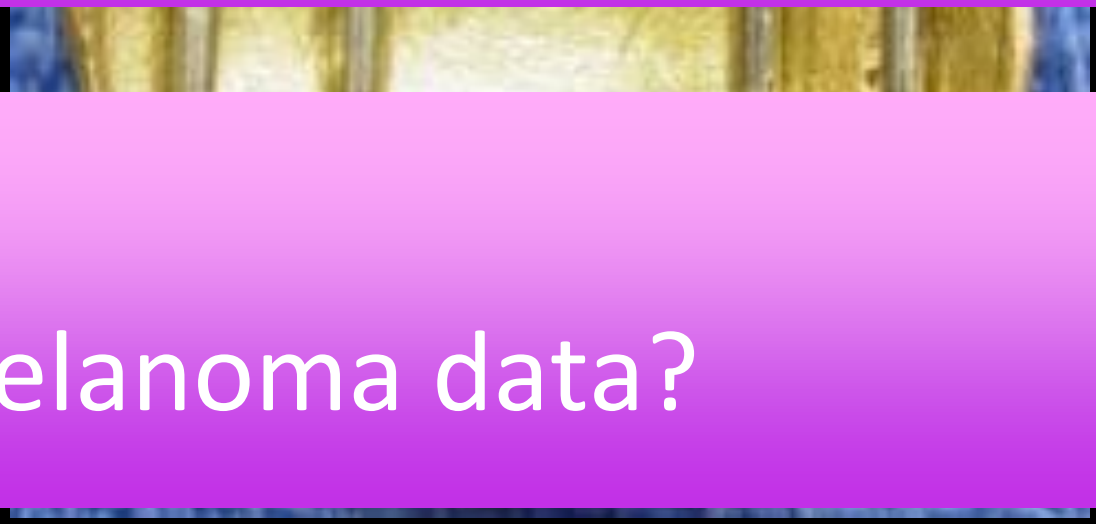

… let’s look at small melanoma data?

- Scleral necrosis

JAMA Ophthalmology | Original Investigation 2018

Visual Outcome and Millimeter Incremental Risk of Metastasis in 1780 Patients With Small Choroidal Melanoma Managed by Plaque Radiotherapy

Carol L. Shields, MD; Kareem Sioufi, MD; Archana Srinivasan, MD; Maura DiNicola, MD; Babak Masoomian, MD; Laura E. Barna, BS, MSc; Vladislav P. Bekerman, BS; Emil A. T. Say, MD; Arman Mashayekhi, MD; Jacqueline Emrich, PhD; Lydia Komarnicky, MD; Jerry A. Shields, MD

IMPORTANCE Early detection of choroidal melanoma at a small tumor size is emphasized in the literature. However, there is little published information on the specific risks of plaque-irradiated small choroidal melanoma on visual acuity and metastasis.

OBJECTIVE To analyze outcomes of plaque radiotherapy for small choroidal melanoma 3 mm in thickness or less.

DESIGN, SETTING, AND PARTICIPANTS This retrospective noncomparative series at a tertiary referral center included 1780 consecutive patients who had received plaque radiotherapy treatment for small choroidal melanoma.

MAIN OUTCOMES AND MEASURES Visual acuity outcomes and melanoma-associated

Invited Commentary
page 1333

Supplemental content and
Journal Club Slides

JAMA Ophthalmology | Original Investigation 2018

Visual Outcome and Millimeter Incremental Risk of Metastasis in 1780 Patients With Small Choroidal Melanoma Managed by Plaque Radiotherapy

Retrospective review of small choroidal melanoma (≤3 mm th) treated with plaque radiotherapy [n=1780 eyes]

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JAMA Ophthalmology | Original Investigation 2018

Visual Outcome and Millimeter Incremental Risk of Metastasis in 1780 Patients With Small Choroidal Melanoma Managed by Plaque Radiotherapy

Retrospective review of small choroidal melanoma (≤3 mm th) treated with plaque radiotherapy [n=1780 eyes]

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MAIN OUTCOMES AND MEASURES Visual acuity outcomes and melanoma-associated

Summary

Following plaque radiotherapy for small uveal melanoma

- KM 10-year rate of mets ~ 10%
- KM 10-year rate of poor Va ~ 50% - ≤20/200
- KM 10-year rate of Va loss ~ 50% - ≥3 Snellen lines
- KM 10-year rate of neovasc = 3%

Treating Small Choroidal Melanoma

Smaller Is Better

JAMA Ophthalmology

2018

H. Culver Boldt, MD; Elaine Binkley, MD

Over the last several decades, ocular oncologists have set a goal to identify and treat smaller uveal melanomas. Another way to rephrase this goal would be to state that we want to identify melanocytic lesions that are likely to spread at some future time and ablate them before they do so. Ocular oncologists are very accurate in diagnosing medium and large uveal melanomas. Differentiation of small melanomas from high-risk choroidal nevi has been more challenging. Approximately 8% of people in the United States have a choroidal nevus. The malignant transformation rate is estimated at about 1 in 9000 per year.[1] This translates into about 2400 new cases of uveal melanoma each year in the United States, and the incidence seems to be increasing. Only about 30% of these lesions are diagnosed while they are small melanomas.

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So how does one differentiate the occasional small uveal melanoma from the thousands of benign choroidal nevi? In the past, significant documented growth of a small lesion often was used as a surrogate for malignant transformation. However, in a study of risk factors for metastasis,[2] growth of a lesion was associated with an 8-fold increase in metastasis. Identification of those lesions that will grow in the future is the goal. In addition,

Treating Small Choroidal Melanoma
Smaller Is Better

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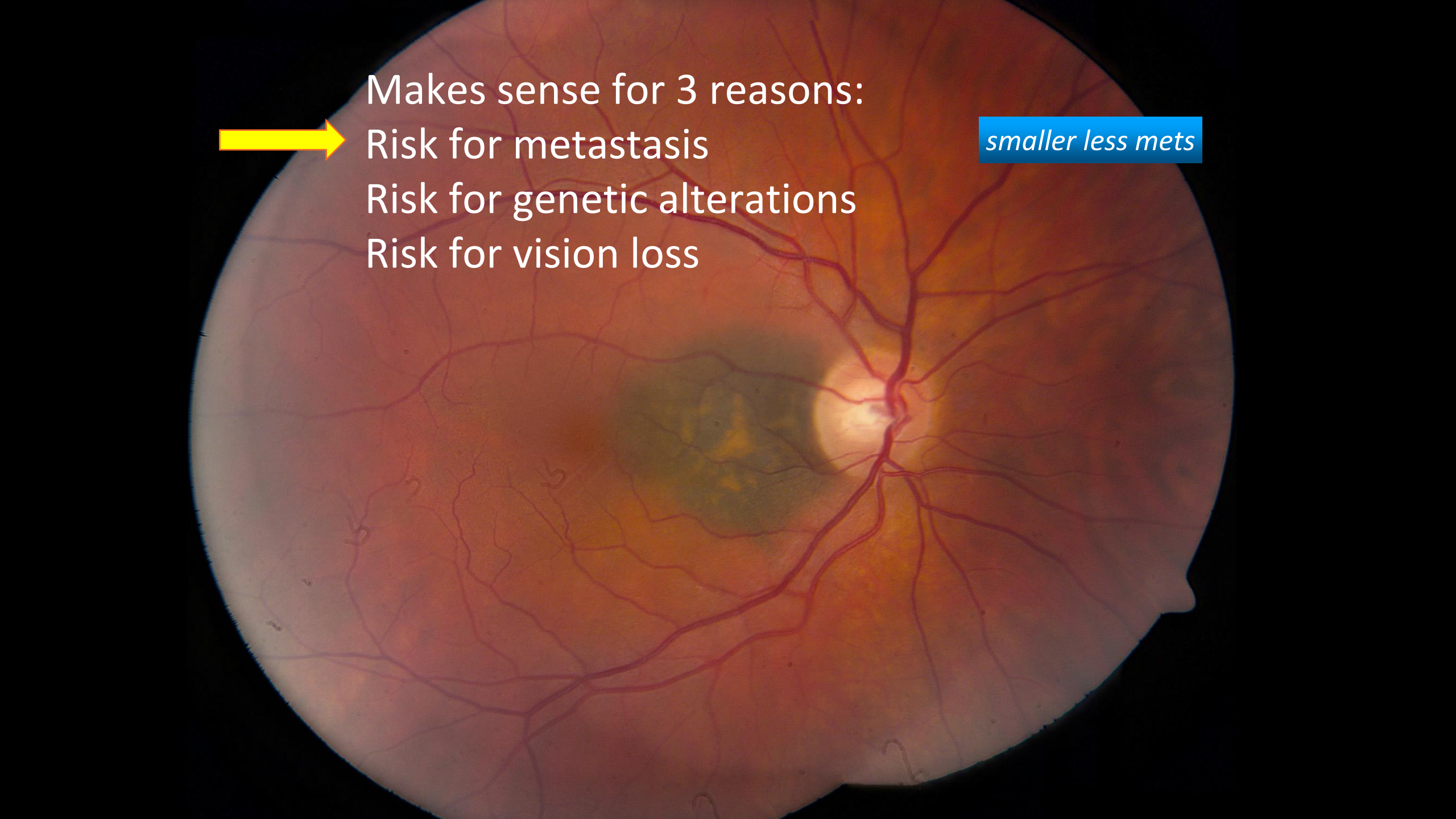
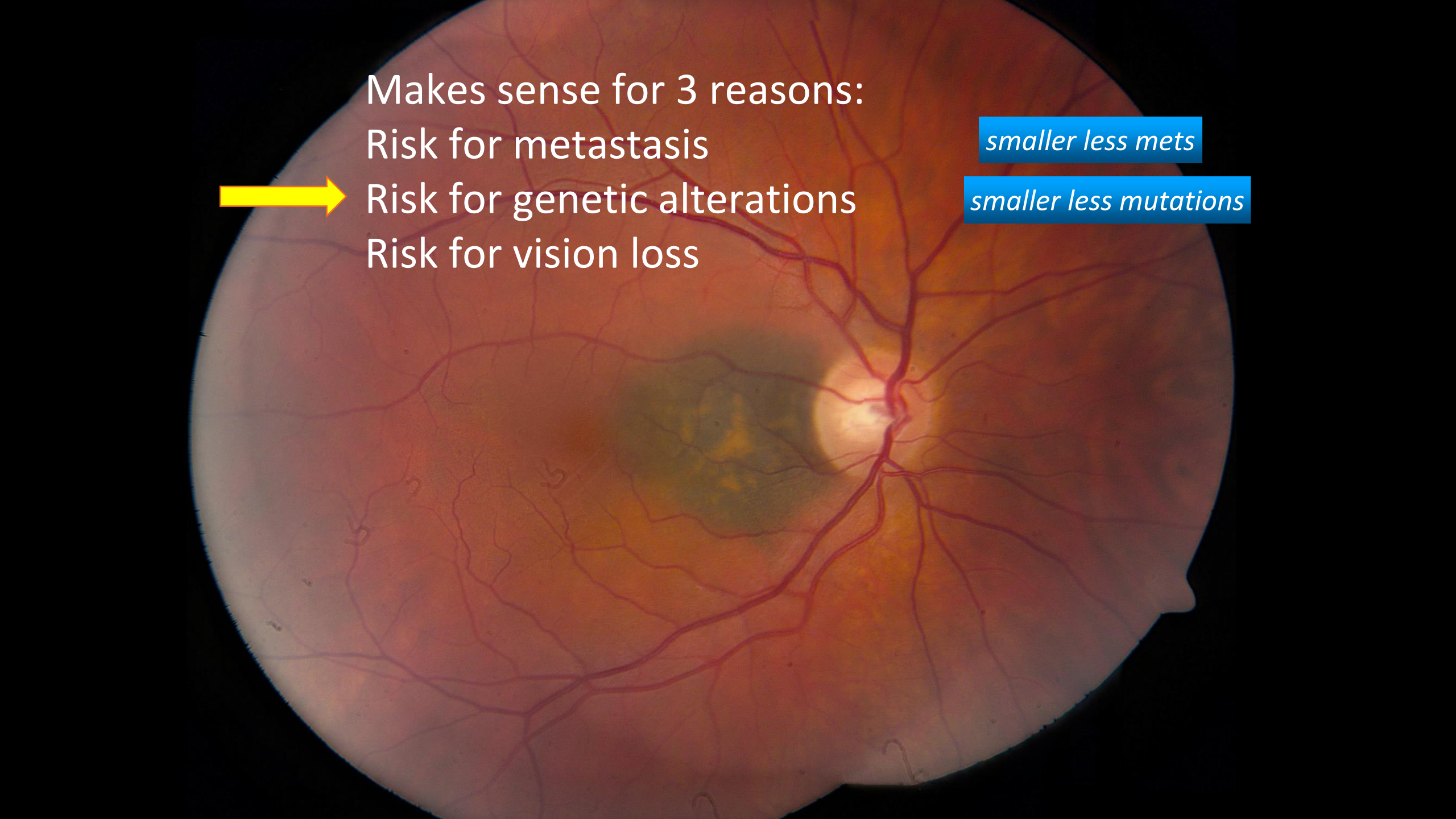
Experts agree: “Smaller is better”

“Treat early to prevent metastasis”


Makes sense for 3 reasons:
Risk for metastasis
Risk for genetic alterations
Risk for vision loss
smaller less mets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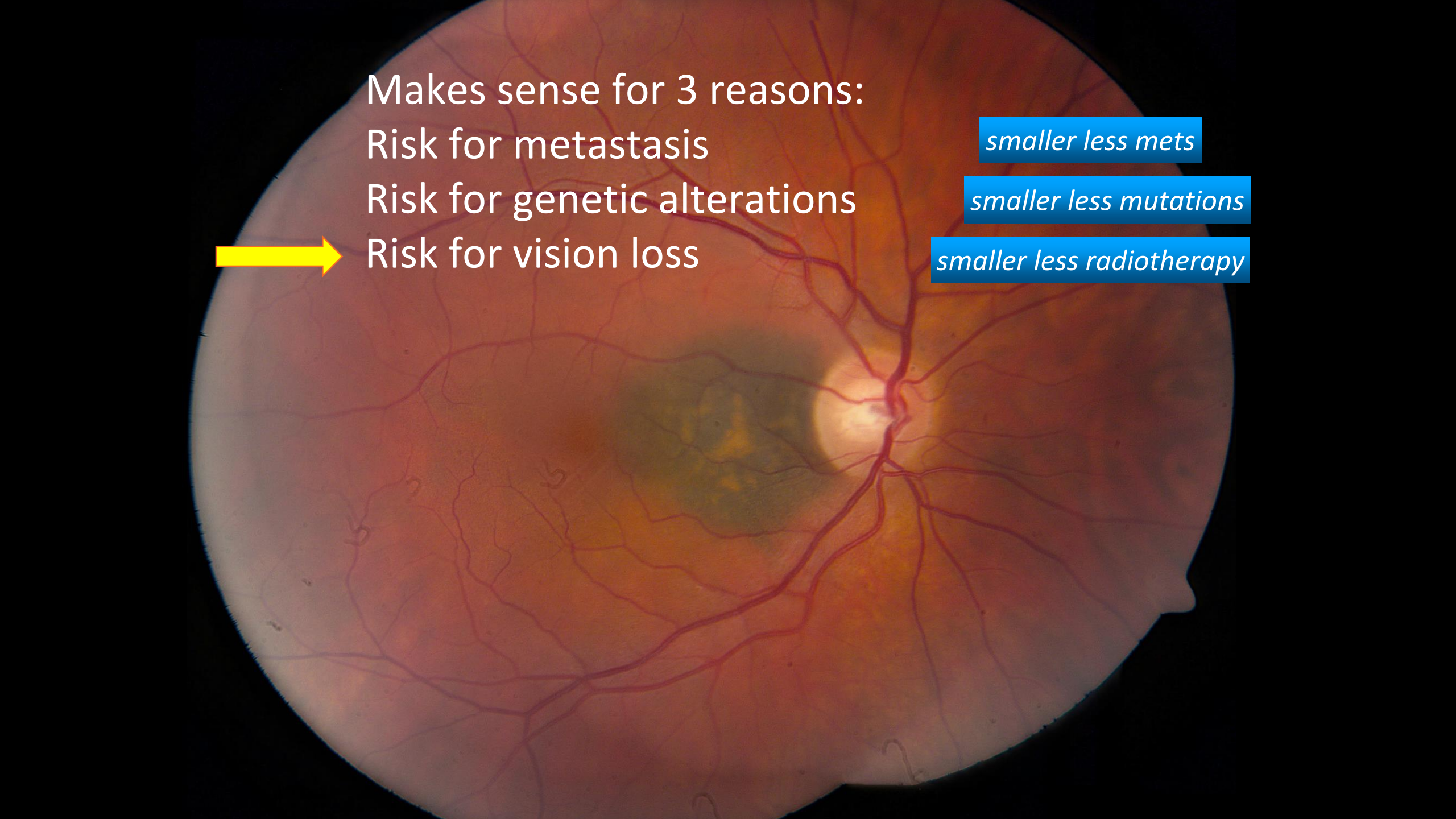
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Metastasis of Uveal Melanoma Millimeter-by-Millimeter in 8033 Consecutive Eyes

Carol L. Shields, MD; Minoru Furuta, MD; Archana Thangappan, MD; Saya Nagori, MD; Arman Mashayekhi, MD; David R. Lally, MD; Cecilia C. Kelly, MD; Danielle S. Rudich, MD; Anand V. Nagori, MD; Oojwala A. Wakade, MD; Sonul Mehta, MD; Lauren Forte, BS; Andrew Long, BS; Elaina F. Dellacava, MD; Bonnie Kaplan, MD; Jerry A. Shields, MD

Objective: To determine the rate of metastasis of uveal melanoma on the basis of tumor thickness in millimeters.

Methods: Retrospective medical record review.

Results: The mean (median) patient age was 58 (59) years. A total of 8033 eyes were examined. Of the 285 eyes with iris melanoma, the mean tumor thickness was 2.7 mm and metastasis occurred in 0.5%, 4%, and 7% at 3, 5, and 10 years, respectively. Of the 492 eyes with ciliary body melanoma, the mean tumor thickness was 6.6 37% for medium melanoma (3.1-8.0 mm), and 35%, 49%, and 67% for large melanoma (>8.0 mm). More specifically, metastasis per millimeter increment at 10 years was 6% (0-1.0 mm thickness), 12% (1.1-2.0 mm), 12% (2.1-3.0 mm), 16% (3.1-4.0 mm), 27% (4.1-5.0 mm), 28% (5.1-6.0 mm), 29% (6.1-7.0 mm), 41% (7.1-8.0 mm), 50% (8.1-9.0 mm), 44% (9.1-10.0 mm), and 51% (>10.0 mm). Clinical factors predictive of metastasis by multivariate analysis included increasing patient age, ciliary body location, increasing tumor diameter, increasing tumor thickness, having a brown tumor, and the presence of sub-

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Tumor Thickness, mm	10 y
Using 1-mm increments	
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1.1-2.0	12.5 (8-17)
2.1-3.0	11.9 (9-15)
3.1-4.0	16.5 (13-20)
4.1-5.0	26.4 (21-32)
5.1-6.0	28.4 (22-35)
6.1-7.0	28.2 (21-36)
7.1-8.0	40.6 (33-49)
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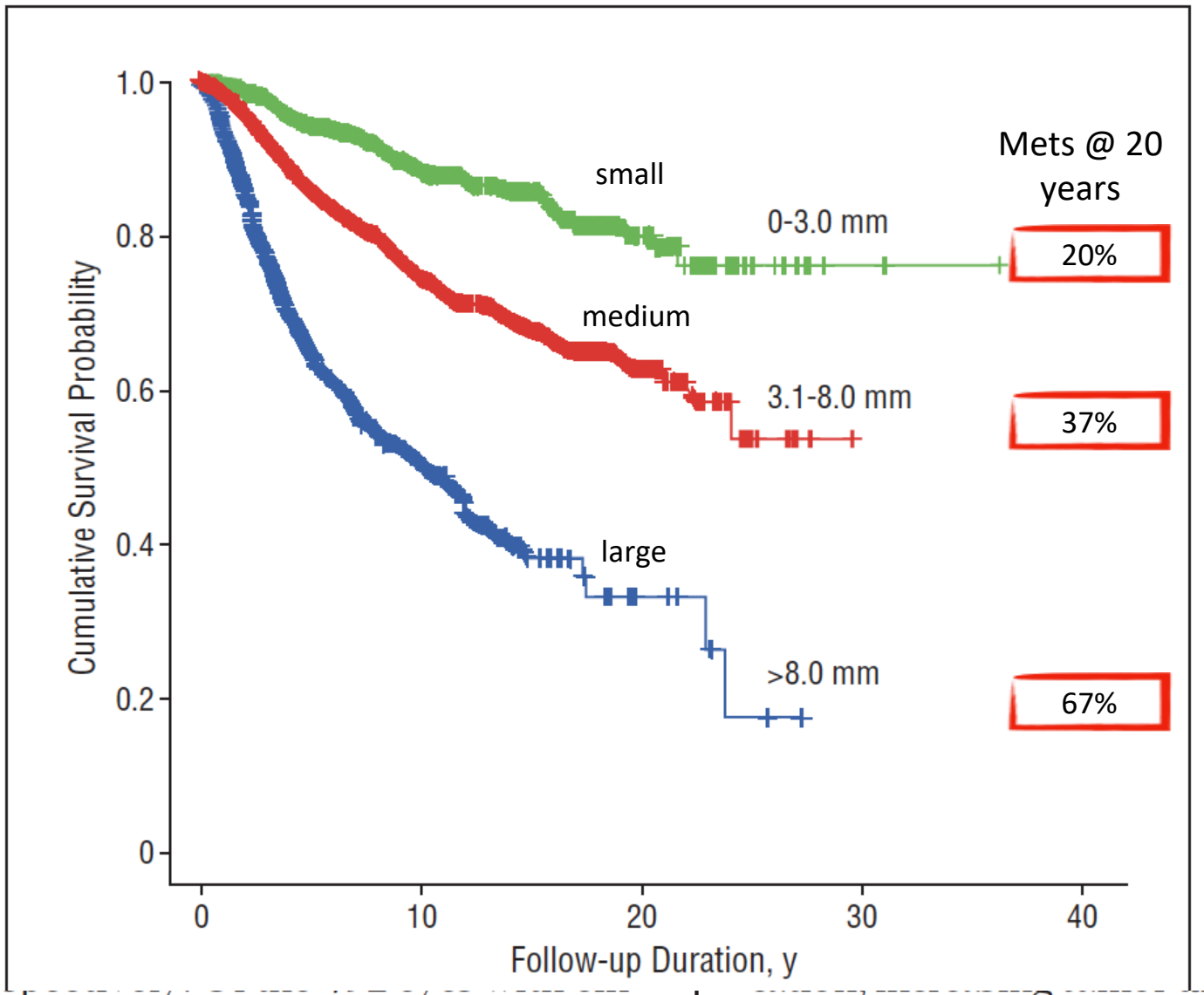

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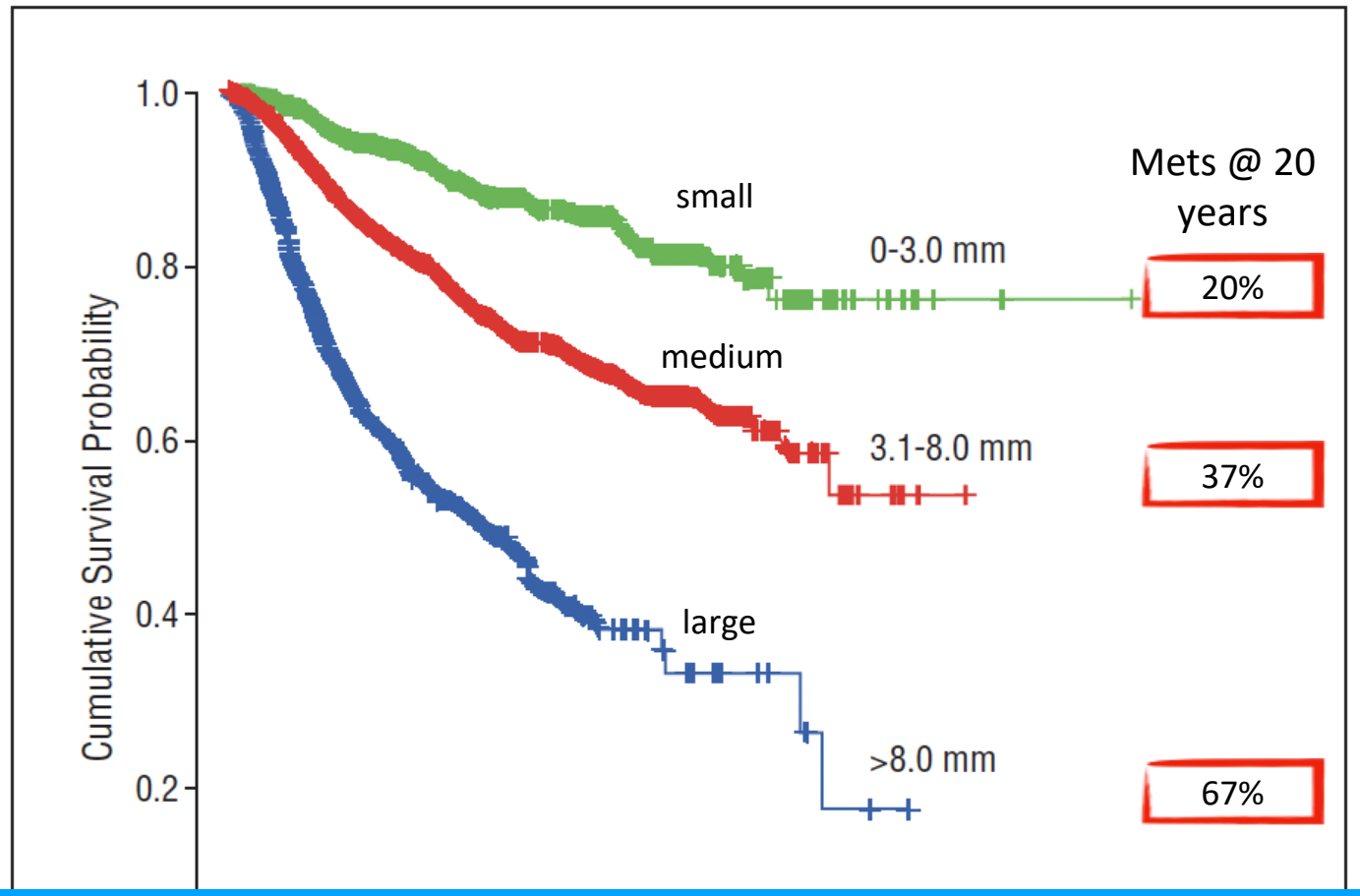

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Smaller is better

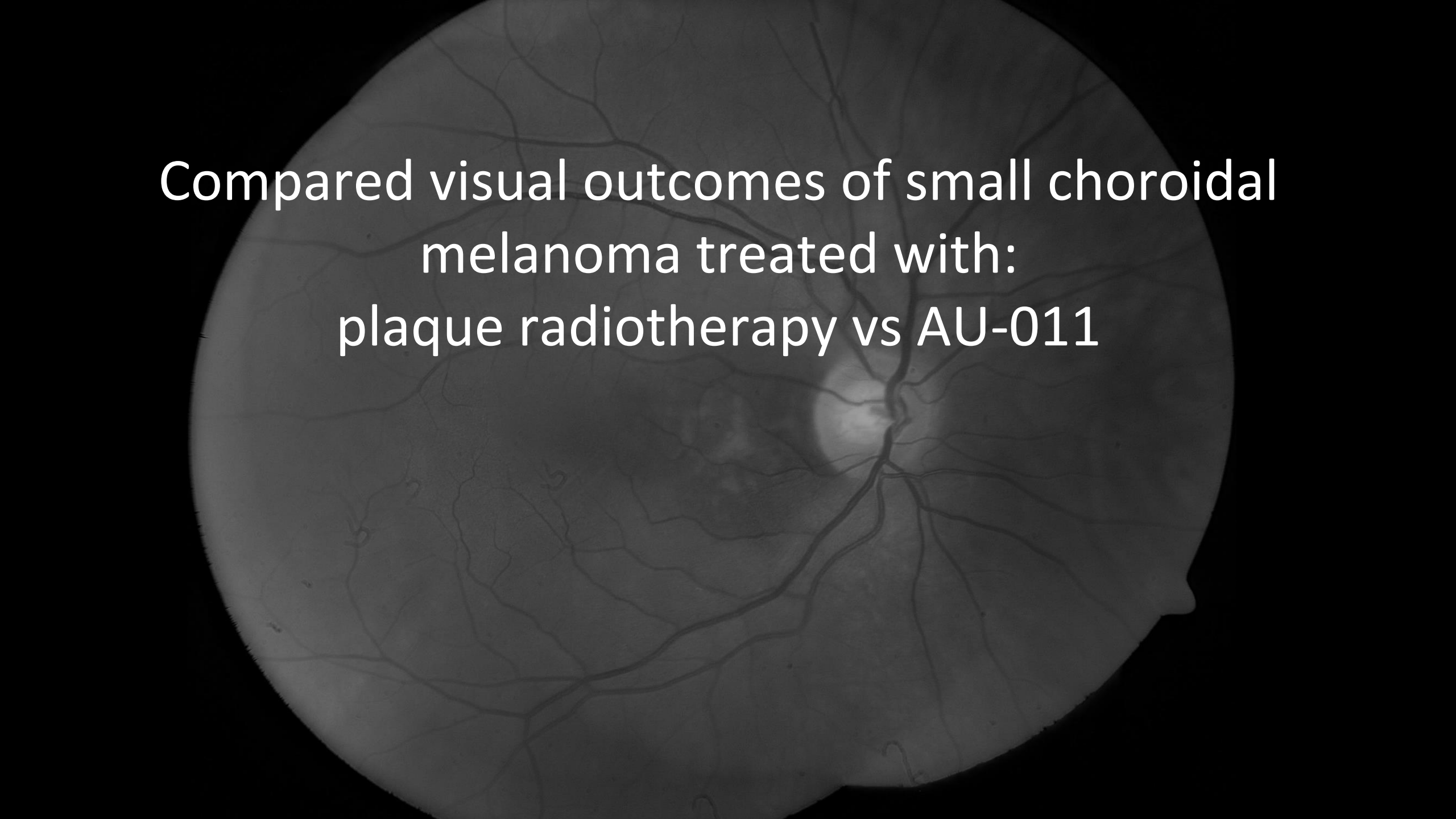
So what are we waiting for …

- challenge differentiating nevus vs melanoma
- plaque radiotherapy can impact vision
- need new therapy that does not impact vision

Treatment of uveal melanoma is *BEST* when the tumor is small

90% survival with a 2.5 mm tumor is better than

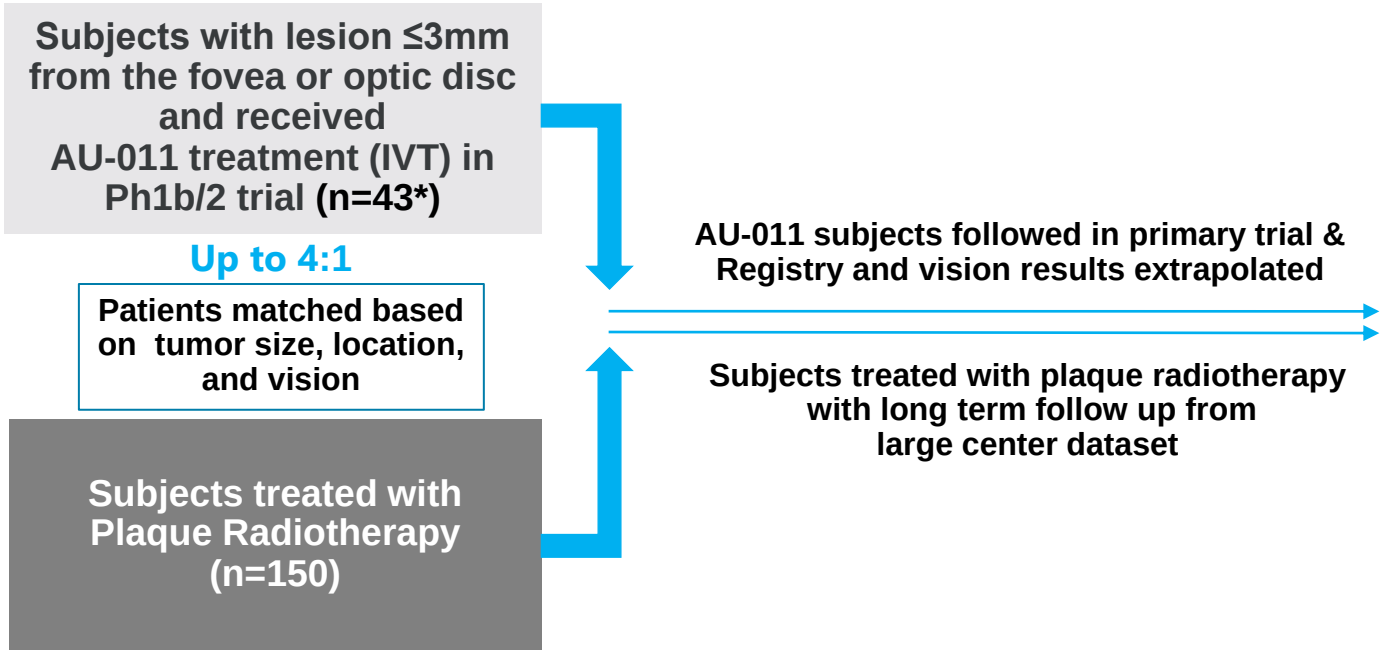
50% survival with a 10 mm tumor



Compared visual outcomes of small choroidal melanoma treated with: plaque radiotherapy vs AU-011

rMCC Study to Evaluate Visual Acuity Outcomes of Belzupacap Sarotalocan [Bel-Sar] vs. Plaque Radiotherapy

- Matching criteria: baseline tumor thickness, LBD, distance to fovea/ optic disc, visual acuity (all 4 must match)
- Matching performed by Independent Statistician
- Comparing 1- and 2-year AU-011 data (2-year data extrapolated for years 3, 4, and 5) to 5 years of retrospective plaque results



Data from patients treated with AU-011 in the Ph1b/2 study and further followed in Registry study will be compared to patients treated with plaque radiotherapy at 1, 2, 3, 4 and 5 years and at last follow up to support visual acuity benefit

Limitations
- Retrospective matched case control design
- Single site database
- Extrapolate AU-011 data from year 2

*43 AU-011 subjects included in matching; 2 AU-011 subjects did not have any matches; results presented for 41 AU-011 subjects with at least 1 match

AU-011 has the Potential to Have Long Term Visual Acuity Benefit over Plaque Radiotherapy

rMCC – retrospective matched case control

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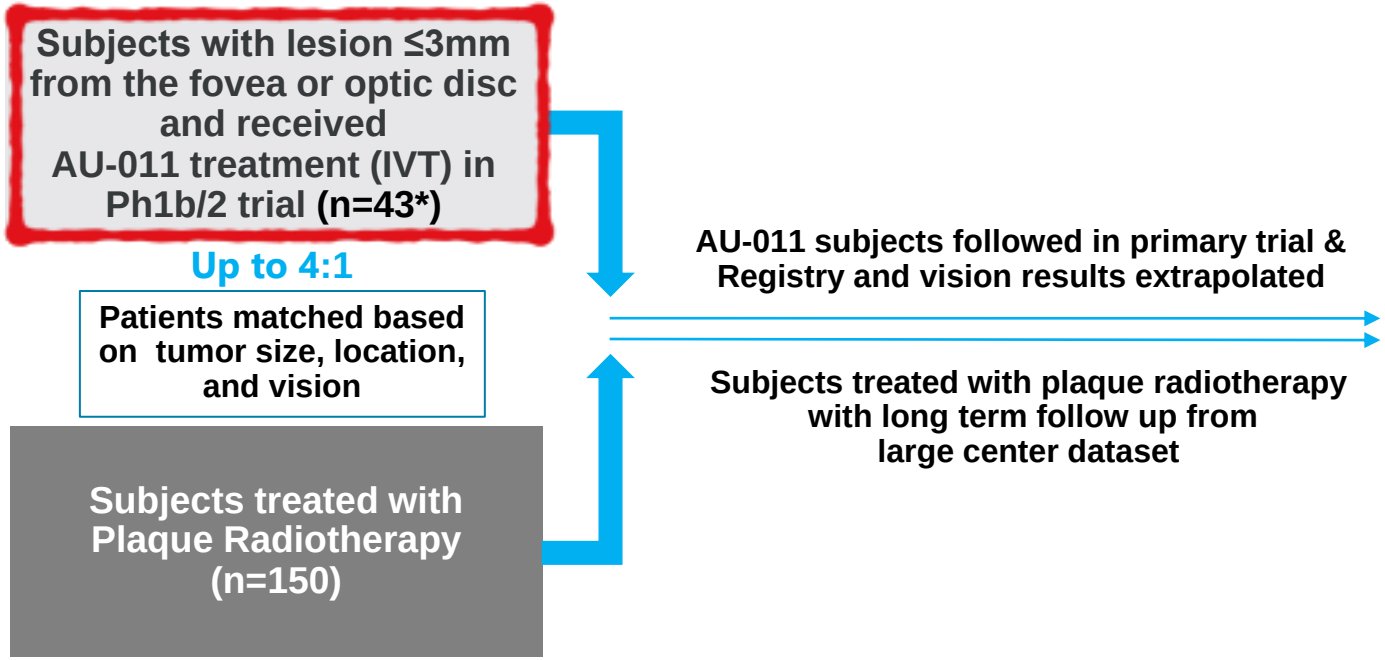

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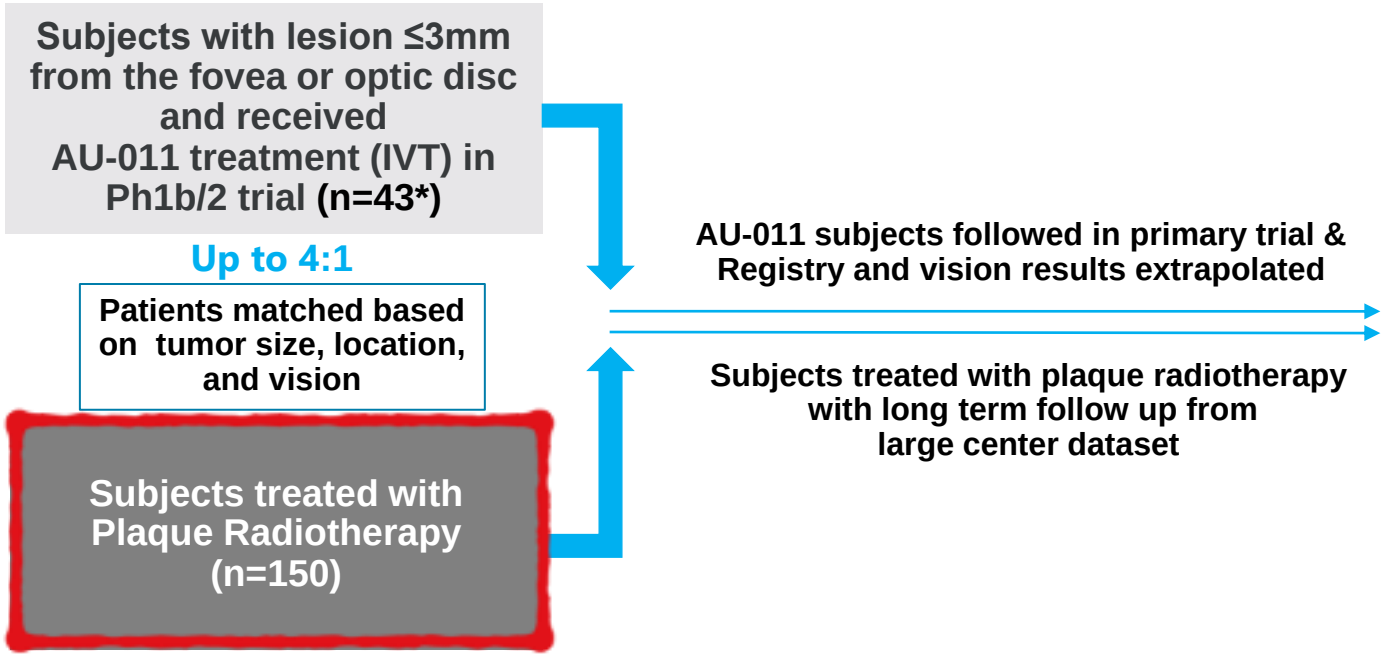

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Study Baseline Demographics

Endpoint	Belzupacap Sarotalocan Subjects N=43		Plaque Radiotherapy Subjects N=150	
Baseline Age (years)				
N	43		150	
Mean (StdDev)	54.8 (13.7)		54.3 (12.8)	
Min., Max.	27.0, 83.0		10.0, 86.0	
Sex	n	Percent	n	Percent
Female	18	41.9	72	48.0
Male	25	58.1	78	52.0
Race	n	Percent	n	Percent
Asian	0	-	1	0.7
Black	1	2.3	0	-
Hispanic	0	-	2	1.3
White	42	97.7	147	98.0

Baseline Demographics Similar Between Belzupacap Sarotalocan and Plaque Subjects

StdDev: standard deviation

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Baseline Matching Characteristics

	AU-011 Subjects (N=43)					Matched Plaque Patients (N=150)				
Endpoint	Mean	Std Dev	Min.	Med.	Max.	Mean	Std Dev	Min.	Med.	Max.
Baseline LogMAR	0.087	0.200	-0.260	0.040	0.620	0.145	0.154	0.000	0.100	0.700
Baseline Distance from optic nerve	2.289	1.883	0.000	2.165	6.280	1.643	1.567	0.000	1.500	6.000
Baseline Distance from fovea	2.183	2.016	0.000	1.440	7.330	1.274	1.640	0.000	0.500	7.000
Baseline Tumor Thickness	2.108	0.537	1.033	2.100	3.400	2.396	0.466	1.200	2.400	3.400
Baseline LBD	8.645	2.103	4.805	8.180	13.350	8.315	2.187	4.000	8.000	13.500

20/25

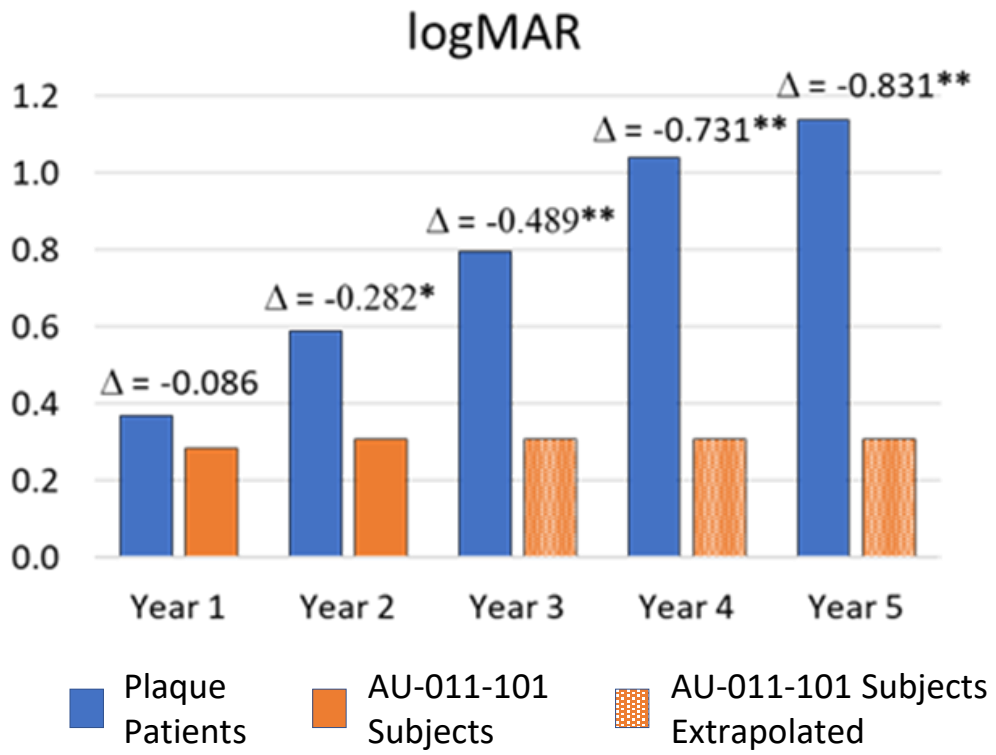
20/25

Matching Characteristics Included Tumor Size, Distance to Fovea or Nerve, and Visual Acuity

LBD: linear basal diameter of tumor; Max: maximum; Med: median; Min: minimum; StdDev: standard deviation

aura

rMCC Results – Statistically Significant Vision Preservation with Belzupacap Sarotalocan vs Plaque Radiotherapy – logMAR^ Vision



* p < 0.05; ** p < 0.001

^logMAR – logarithm of the minimal angle of resolution

logMAR Visual Acuity – AU-011 vs Plaque

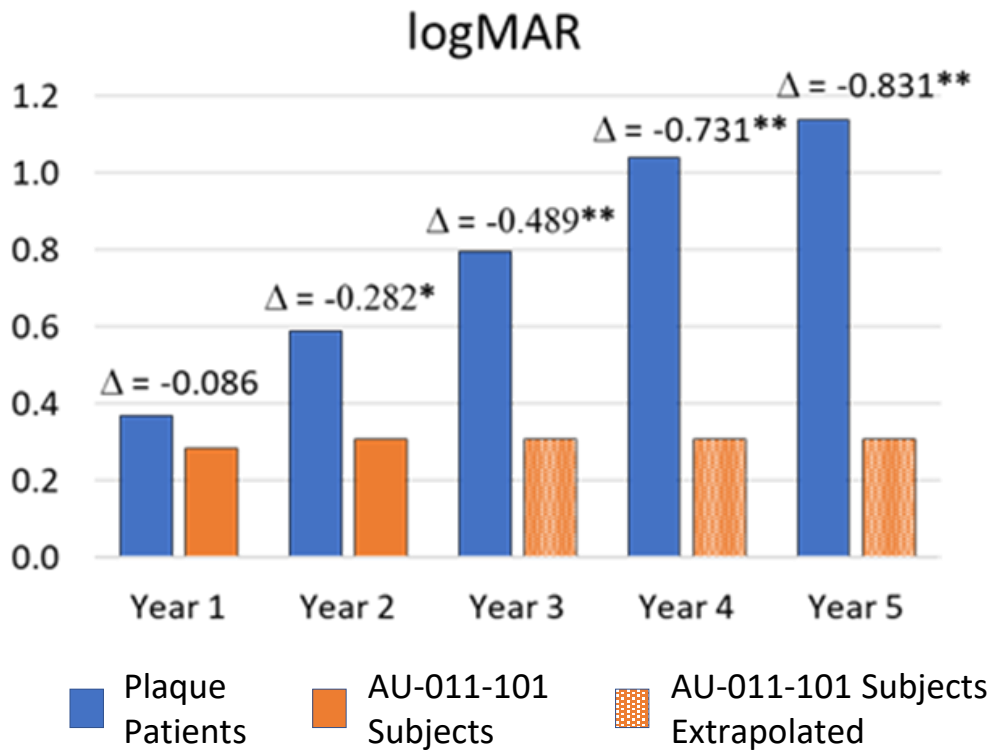
AU-011 Timepoint	Plaque Timepoint	Multiple Imputation Method			
		LS-Means AU-011	LS-Means Plaque	LS-Means Treatment Difference	p-value
Year 1	Year 1	0.283	0.369	-0.086	0.3415
Year 2	Year 2	0.307	0.589	-0.282	0.0183
Year 2	Year 3	0.307	0.796	-0.489	0.0002
Year 2	Year 4	0.307	1.038	-0.731	<.0001
Year 2	Year 5	0.307	1.138	-0.831	<.0001

- Mixed model repeated measures (MMRM) analysis controlling for matching.
- n=41 AU-011 subjects compared to n=148 matched plaque patients
- Multiple imputation to address missing data.

Statistically Significant Vision Preservation Starting at 2 Years

aura

rMCC Results – Statistically Significant Vision Preservation with Belzupacap Sarotalocan vs Plaque Radiotherapy – logMAR^ Vision



* p < 0.05; ** p < 0.001

^logMAR – logarithm of the minimal angle of resolution

logMAR Visual Acuity – AU-011 vs Plaque

AU-011 Timepoint	Plaque Timepoint	Multiple Imputation Method			
		LS-Means AU-011	LS-Means Plaque		p-value
Year 1	Year 1	20/40	20/50		0.3415
Year 2	Year 2	20/40	20/80		0.0183
Year 2	Year 3	20/40	20/120		0.0002
Year 2	Year 4	20/40	20/200		<.0001
Year 2	Year 5	20/40	<20/200		<.0001

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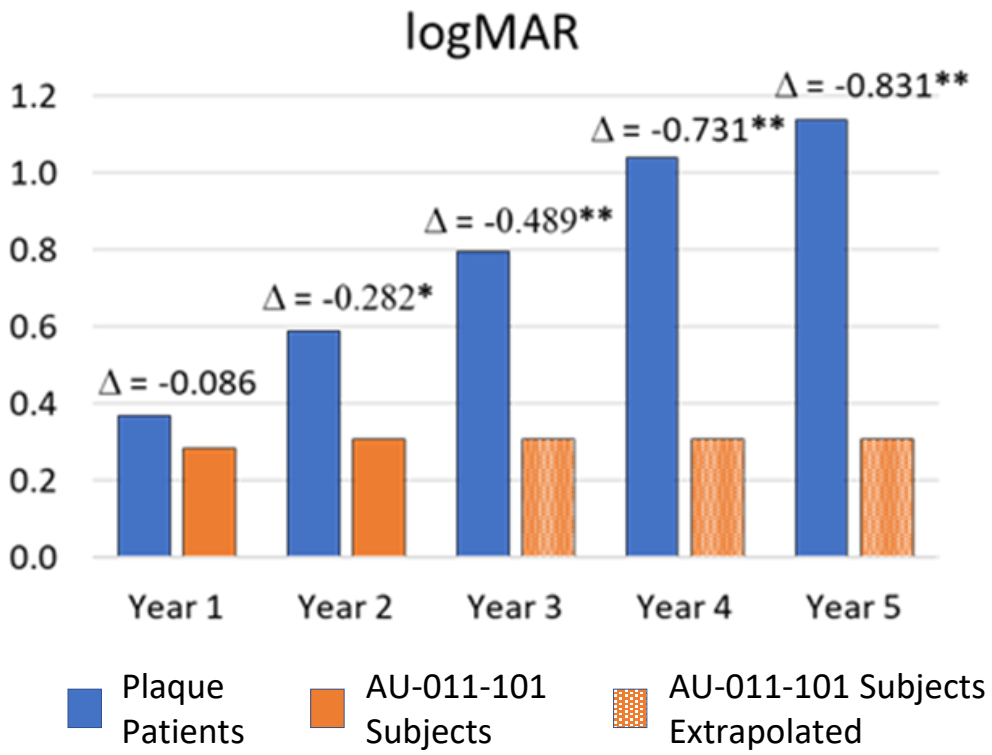

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		LS-Means AU-011	LS-Means Plaque	LS-Means Treatment Difference	p-value
Year 1	Year 1	20/40	20/50	-0.086	0.3415
Year 2	Year 2	20/40	20/80	-0.282	0.0183
Year 2	Year 3	20/40	20/120	-0.489	0.0002
Year 2	Year 4	20/40	20/200	-0.731	<.0001
Year 2	Year 5	20/40	<20/200	-0.831	<.0001

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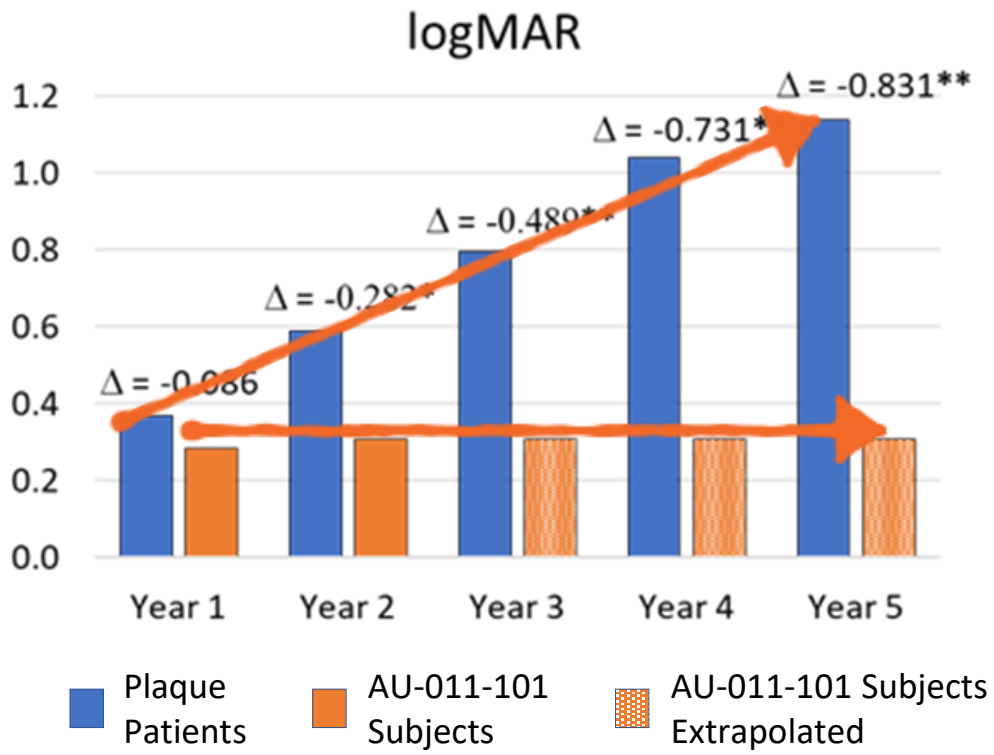

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Loss of Lines of logMAR Vision Statistically Significant by 3 Years

AU-011 Timepoint	Plaque Timepoint	Loss of logMAR ≥ 0.3			Loss of logMAR ≥0.6		
		Plaque (%)	AU-011 (%)	p-value	Plaque (%)	AU-011 (%)	p-value
Year 1	Year 1	25.6%	25.6%	0.5155	12.3%	10.7%	0.5120
Year 2	Year 2	42.6%	30.0%	0.3261	26.1%	16.0%	0.4977
Year 3	Year 3	53.5%	30.0%	0.0312	35.6%	16.0%	0.0718
Year 4	Year 4	66.8%	30.0%	0.0002	54.0%	16.0%	0.0002
Year 5	Year 5	73.4%	30.0%	<.0001	60.1%	16.0%	<.0001

- Analysis of the proportion of subjects with a loss of logMAR ≥ 0.3 and ≥ 0.6 via Cochran–Mantel–Haenszel test to control for matching.
- Multiple imputation to address missing data.
- n=41 AU-011 subjects compared to n=148 matched plaque patients.
- Comparing AU-011-101 & Registry trial values with plaque timepoints.

These Results Point to the High Unmet Medical Need for a First-Line Vision Preserving Therapy for the Treatment of Early-Stage Choroidal Melanoma

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Matched Case Control for UM: AU-011 vs Plaque

- 2-year data confirms that visual acuity after treatment with belzupacap sarotalocan is stable long term
- Highlights the high unmet medical need for a vision preserving therapy for early-stage disease given the visual outcomes with radiotherapy
- Supports the trend for earlier treatment intervention in UM given the progress in identifying key risk factors for early diagnosis
- Belzupacap sarotalocan has the potential to be the first approved therapy for the treatment of indeterminate lesions and small UM

Belzupacap sarotalocan has the potential to be the first approved therapy for the treatment of indeterminate lesions and small choroidal melanoma

Phase 2 Suprachoroidal Safety and Efficacy

A Phase 2 Trial of Belzupacap Sarotalocan (AU-011) A First-in-Class Targeted Therapy for Choroidal Melanoma via Suprachoroidal Administration

Ivana K. Kim, MD, MBA

On Behalf of the AU-011 Investigator Group

Co-Director Ocular Melanoma Center

Massachusetts Eye and Ear

Associate Professor of Ophthalmology

Harvard Medical School

AAO 2022

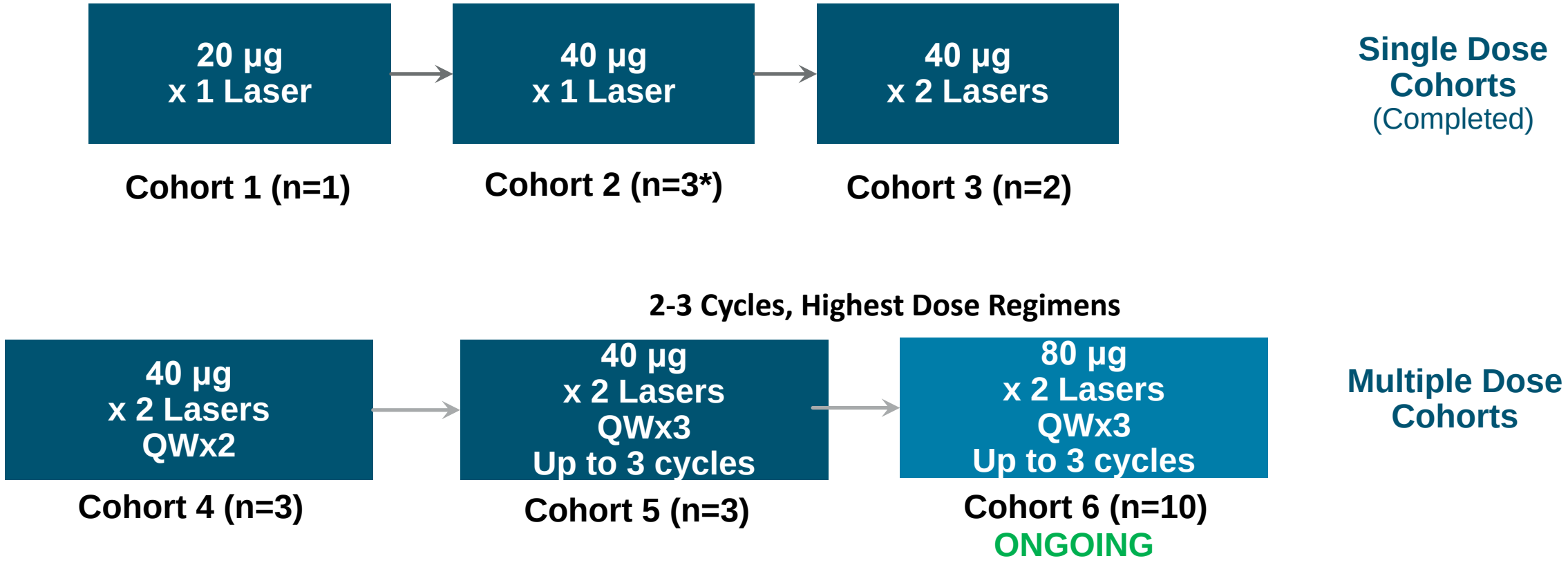
October 2, 2022

AU-011-202, NCT04417530

HARVARD MEDICAL SCHOOL | DEPARTMENT OF Ophthalmology

Phase 2 Trial of Belzupacap Sarotalocan via Suprachoroidal Administration Dose Escalation Study Design

Patient Population: Indeterminate lesions and small choroidal melanoma (IL/CM)
Objective: Determine the optimal dose and therapeutic regimen with suprachoroidal administration



*2 subjects were planned; third subject was additionally enrolled due to dose error in 1 subject

AU-011-202, NCT04417530

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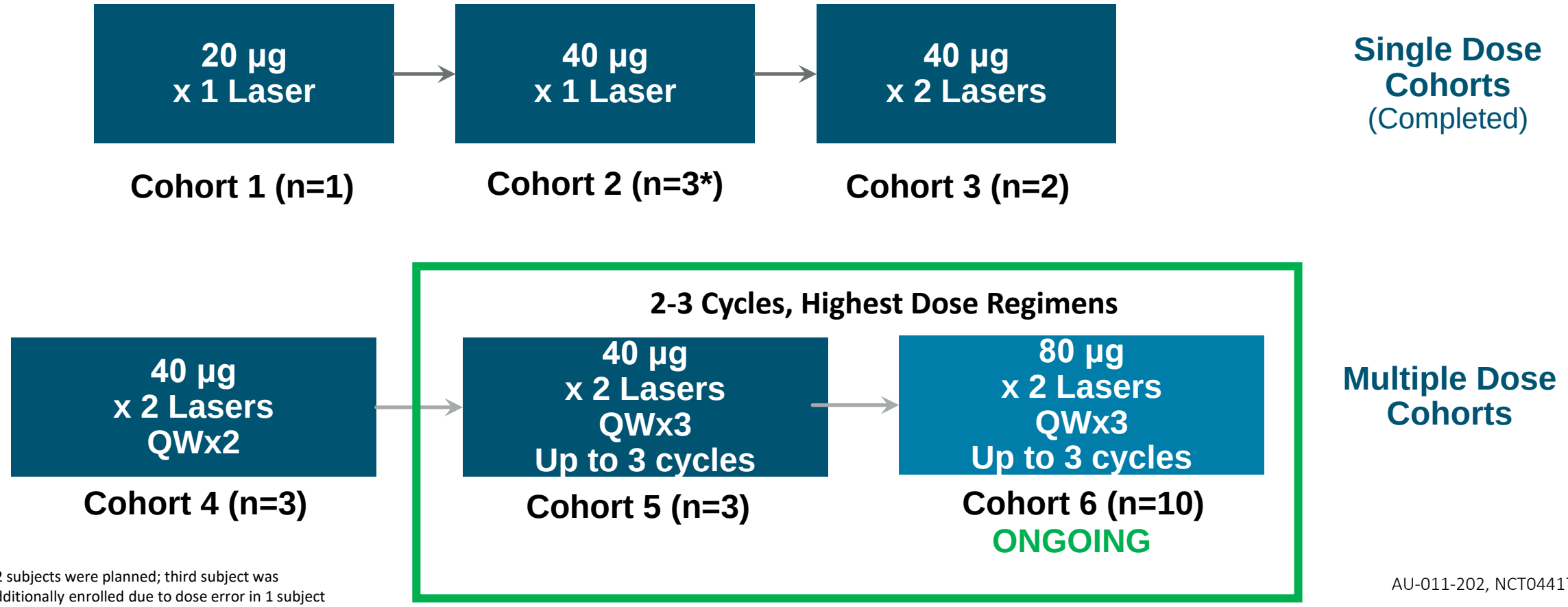

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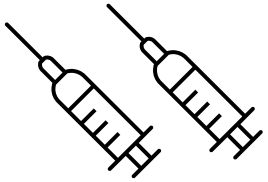
AU-011-202, NCT04417530

Therapeutic Regimen is Completed in 3 Treatment Cycles

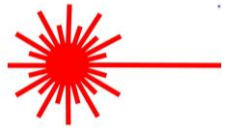
One **treatment** consists of two suprachoroidal injections of belzupacap sarotalocan, followed by two light activations



Belzupacap Sarotalocan Injections

4-4.5mm from the limbus, quadrant of tumor or adjacent quadrant

4-6 Hours Waiting Period



Laser #1

30 Minutes Waiting Period

Laser #2

Therapeutic Regimen is Completed in 3 Treatment Cycles

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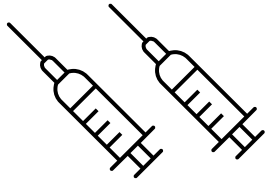


Belzupacap Sarotalocan Injections

4-6 Hours Waiting

Laser #1

30 Minutes Waiting

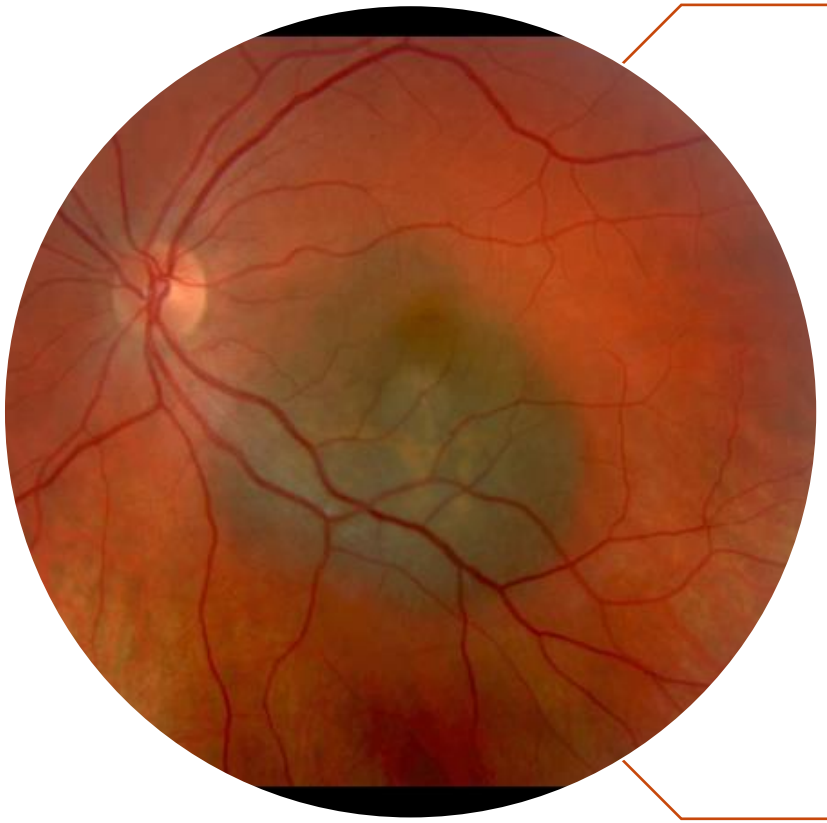
Laser #2

One **cycle** consists of three weekly treatments of belzupacap sarotalocan, followed by one week of no treatment

WEEK	0	1	2	3	4	5	6	7	8	9	10
	☑	☑	☑		☑	☑	☑		☑	☑	☑
	Cycle 1				Cycle 2				Cycle 3		

Patient Population Representative of Early-Stage Disease

Indeterminate Lesions and Small Choroidal Melanoma

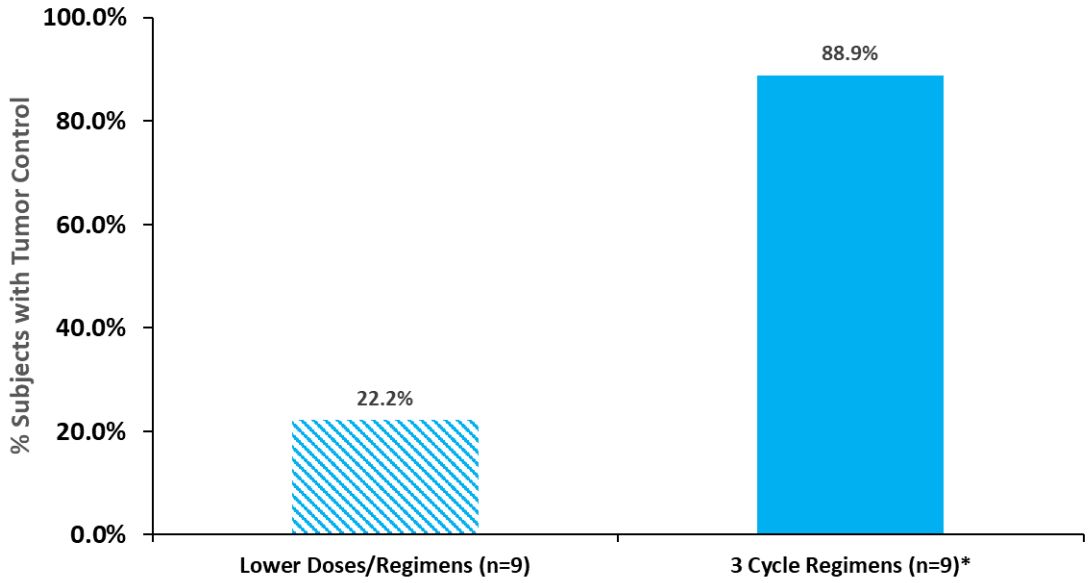


Small Tumors with Documented Growth

- Tumor thickness ≥0.5 mm and ≤2.5 mm
- Largest Basal Diameter (LBD) ≤10 mm
- Documented tumor growth within 2 years of screening
  - Tumor growth rate ≥0.2mm/year

Tumor Control Rates at 6 Months of Follow Up Demonstrate Dose Response

3 Cycle Regimens vs. Lower Regimens



Tumor Progression: change from baseline in thickness ≥0.5mm; or in LBD ≥1.5mm confirmed by at least one repeat assessment

19-Aug-2022 cutoff, interim data

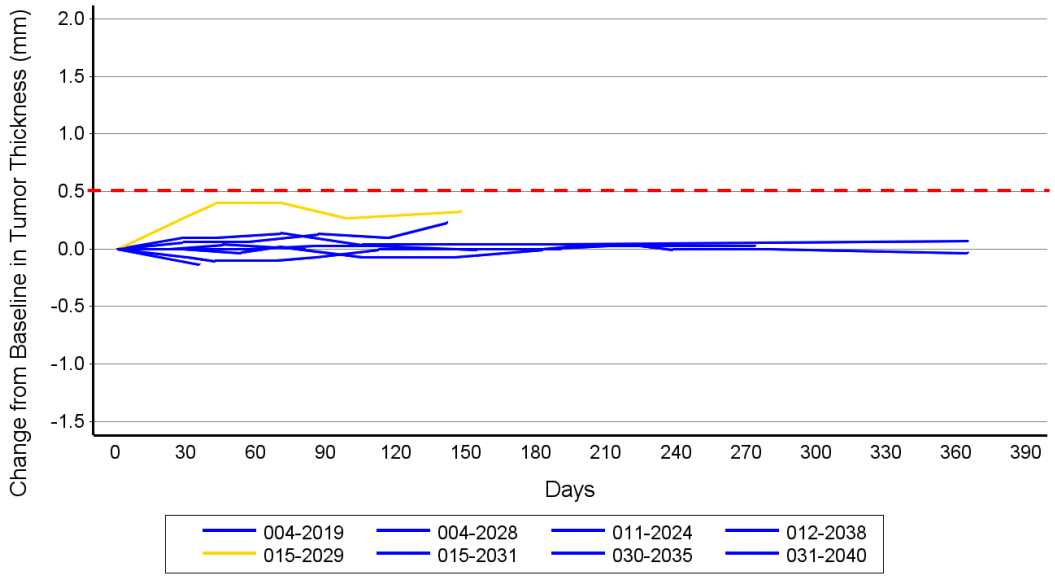
Average 6 Months of Follow Up

Populations	Total Patients (n)	Tumor Control Rate	Average Follow-up (months)
All Doses/Regimens			
All Treated Patients	20	55% (11/20)	8
Lower Doses/Regimens⁺			
Less than 1 cycle	9	22% (2/9)	11
Highest Doses/Regimens*⁺⁺			
2 Cycles (40µg)	1	0% (0/1)	6
3 Cycles (40µg-80µg) 40µg (n=2)/80µg (n=7)	9	**89%** (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
⁺Assigned regimens- less than 1 cycle with doses of 20µg x 1 Laser or 40µg x 1 or 2 Lasers
⁺⁺ Assigned regimens- 2-3 cycles, each cycle comprised of 3 once/week treatments of 40µg x 2Laser or 80µg x 2Laser

Early Analysis of Tumor Control with 3 Cycle Regimen

Therapeutic Regimen (3 cycles)



Change from Baseline in Tumor Thickness Over 12 Months

Progression Definition based on Tumor Thickness (Increase ≥0.5mm)

Subject 015-2029 had circumpapillary tumor – similar subjects will be excluded from pivotal

Ongoing Phase 2 SC trial (AU-011-202), post-SOC data not included

*1 subject without post-baseline tumor thickness data not included in plot

Tumor Control Rate

Population	Total Patients (n)	Tumor Control Rate (%,n)	Average Follow up (months)
Active Growth and Highest dose/Regimen*			
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	89% (8/9)	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

19-Aug-2022 cutoff, interim data

Tumor Progression Definition

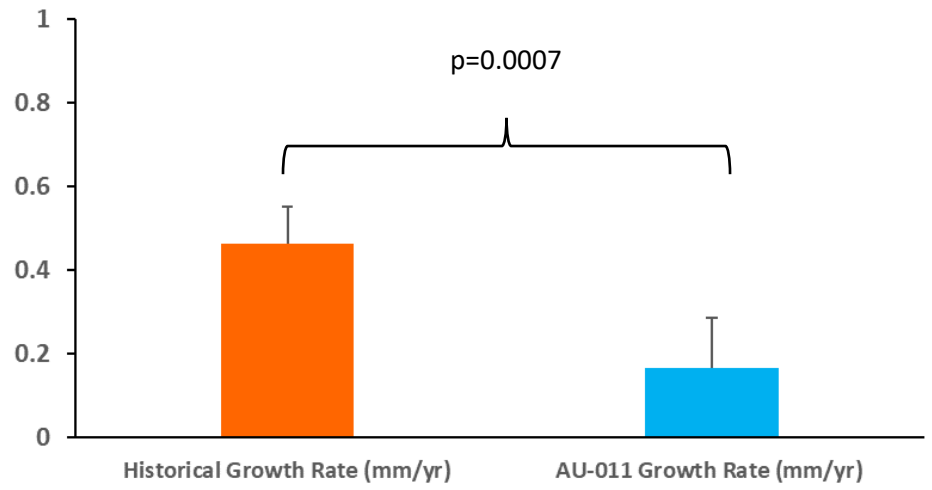
- change from baseline thickness ≥0.5mm

or

- change in LBD ≥1.5mm
- confirmed by at least one repeat assessment

Early Analysis of Tumor Growth Rate with 3 Cycle Regimen

Change in Tumor Growth (mm/yr) 3 Cycle Regimens (n=9)



Change in Tumor Growth

	n	Historical Growth Rate (mm/yr)	AU-011 Growth Rate (mm/yr)	Growth Rate Reduction (mm/yr)	p-value	Average Follow up (months)
Active Growth and Highest Dose/Regimen*						
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	0.463	0.166	-0.296	0.0007	6

Tumor thickness growth rates/ slopes estimated using MMRM

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included

19-Aug-2022 cutoff, interim data

Interim Data Shows Statistically Significant Growth Rate Reduction in Subjects Treated with 3 Cycles

Early Analysis of Visual Acuity

Preservation Rate of 89% at the Highest Dose Regimen

Vision Preservation Rates					
Populations	**Total Patients (n)**	**Vision Failures** (n)**	**Vision Preservation Rate**	**Mean Change from Baseline at Last Visit** (letters)	**Average Follow-up** (months)
All Dose Cohorts					
All Treated Patients	20	2	90%	-3.3	8
High Risk for Vision Loss	15	2	87%	-4.5	7
Highest Doses/Regimens *					
2 Cycles (40µg)	1	0	100%	-3.0	6
3 Cycles (40µg-80µg) 40µg (n=2) 80µg (n=7)	9	1	89%	-3.9	6

*One subject in C6 who discontinued after 1 cycle due to unrelated SAEs is not included
**Confirmed loss ≥15 letters at ≥Week 39; post-SOC data not included
19-Aug-22 cutoff, interim data

Interim Data Shows High Vision Preservation Rates Across All Groups
Including Subjects at High Risk for Vision Loss

Ongoing Safety Evaluation Continues to Be Favorable with No Related SAEs/DLTs Observed to Date

All Treated Subjects (n=20) Treatment Related Adverse Events	Grade I	Grade II	Grade III	Total
Anisocoria	5%	0	0	5%
Anterior chamber cell	5%	0	0	5%
Anterior chamber inflammation	20%	0	0	20%
Conjunctival edema	5%	0	0	5%
Conjunctival hemorrhage	5%	0	0	5%
Conjunctival hyperemia	15%	0	0	15%
Cystoid macular edema	5%	0	0	5%
Eye pain	5%	5%	0	10%
Eyelid edema	5%	0	0	5%
Ocular discomfort	5%	0	0	5%
Photophobia	5%	0	0	5%
Punctate keratitis	10%	0	0	10%
Pupillary reflex impaired	5%	0	0	5%
Retinal pigment epitheliopathy	5%	0	0	5%
Salivary gland enlargement	0	5%	0	5%

19-Aug-2022 data cutoff, interim data
Table presents percentage of subjects with AEs related to AU-011 or laser by severity and overall; subjects with more than 1 AE are counted in the highest severity group

- Majority of AEs were transient and resolved without clinical sequelae
- No DLTs†, no significant vitritis to date through 3 cycles with 80 µg of AU-011
- 4 moderate severity events related to injection procedure - scleritis, subconjunctival hemorrhage, conjunctival edema and eye irritation. All other injection related events were mild
- No discontinuations due to treatment-related AEs
- 6 non-treatment related SAEs reported in 3 subjects^
- No pigmentary changes observed at edge of tumor treatment

- †No dose limiting toxicities or treatment-related SAEs
- ^ 6 SAEs (in 3 subjects) unrelated to AU-011 treatment (retinal detachment, retinal vein occlusion, brain abscess, deep vein thrombosis, sarcoma, seizure)

Ongoing Ph 2 Trial of Suprachoroidal Administration Provides Additional Safety and Efficacy Data

Supports Potential Treatment of Early-Stage Disease

Safety	Mild to moderate treatment-related AEs overall and no related SAEs/DLTs observed to date
Visual Acuity	Visual acuity preservation rate of 87-90% even in subjects with tumors close to the fovea or optic disc
Tumor Control	Early outcomes have shown high tumor control rate (89%) with approximately 6 months average follow up in subjects treated with the therapeutic regimen
Tumor Thickness Growth Rate	Statistically significant reduction in early analysis of tumor growth rates (p=0.0007)
Low to No Intraocular Inflammation	Minimal anterior uveitis and no vitritis observed to date No pigmentary changes
Route of Administration	Initial safety and efficacy data in this ongoing Ph2 trial support SC administration as a potential route

Study ongoing/interim data with Aug 19, 2022 cut off

Belzupacap Sarotalocan Ocular Oncology Investigator Group

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Philadelphia, PA

Dr. Ivana Kim
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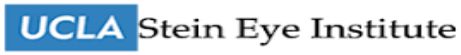
New York, NY

Dr. Hakan Demirci
Ann Arbor, MI



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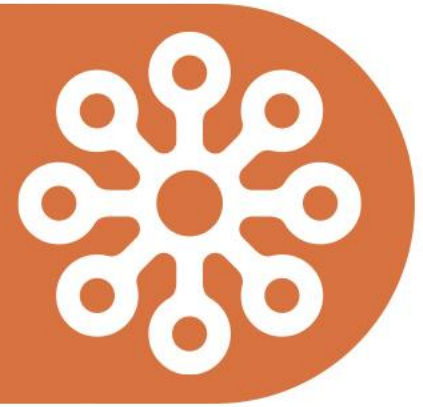
San Francisco, CA

Moderated Q&A



aura

Moderated Q&A Guest Speakers

Martine Jager, MD, PhD

Professor of Ophthalmology, Leiden University, (Netherlands) & Past President of the International Society of Ocular Oncology and the Association for Research in Vision and Ophthalmology

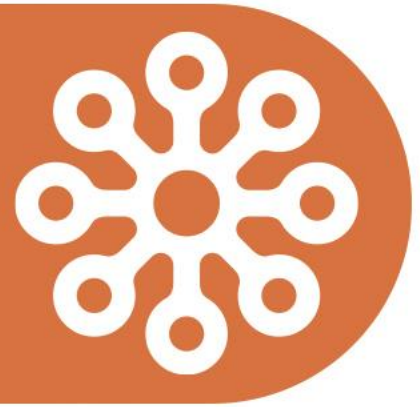
Carol Shields, MD

Chief of the Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University (Philadelphia, PA)

Ivana Kim, MD, MBA

Director of the Ocular Melanoma Center, Massachusetts Eye and Ear & Associate Professor of Ophthalmology, Harvard Medical School (USA)

Audience Q&A



Thank you for attending