

AMD MANAGEMENT ...

What changes with a new player



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Financial Disclosure

- **CONSULTANT** [*Alcon, Bayer, Novartis*]
- **CLINICAL TRIALS/STUDIES** [*Alcon, Allergan, Angelini, Bayer, Sensimed, Thea*]
- **GRANT SUPPORT** [*Abbvie, Alcon, Bausch&Lomb, Bayer, Carl Zeiss, Heidelberg, Novartis, Sensimed, Thea, Topcon*]

AMD MANAGEMENT ...

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AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES

IDENTIFICATION AND MANAGEMENT OF RESISTANT NEOVASCULAR AMD

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

AMD MANAGEMENT ...



What changes with a new player

- The gold-standard diagnostic technique for the diagnosis and classification is ... FLUORESCEIN ANGIOGRAPHY

AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES

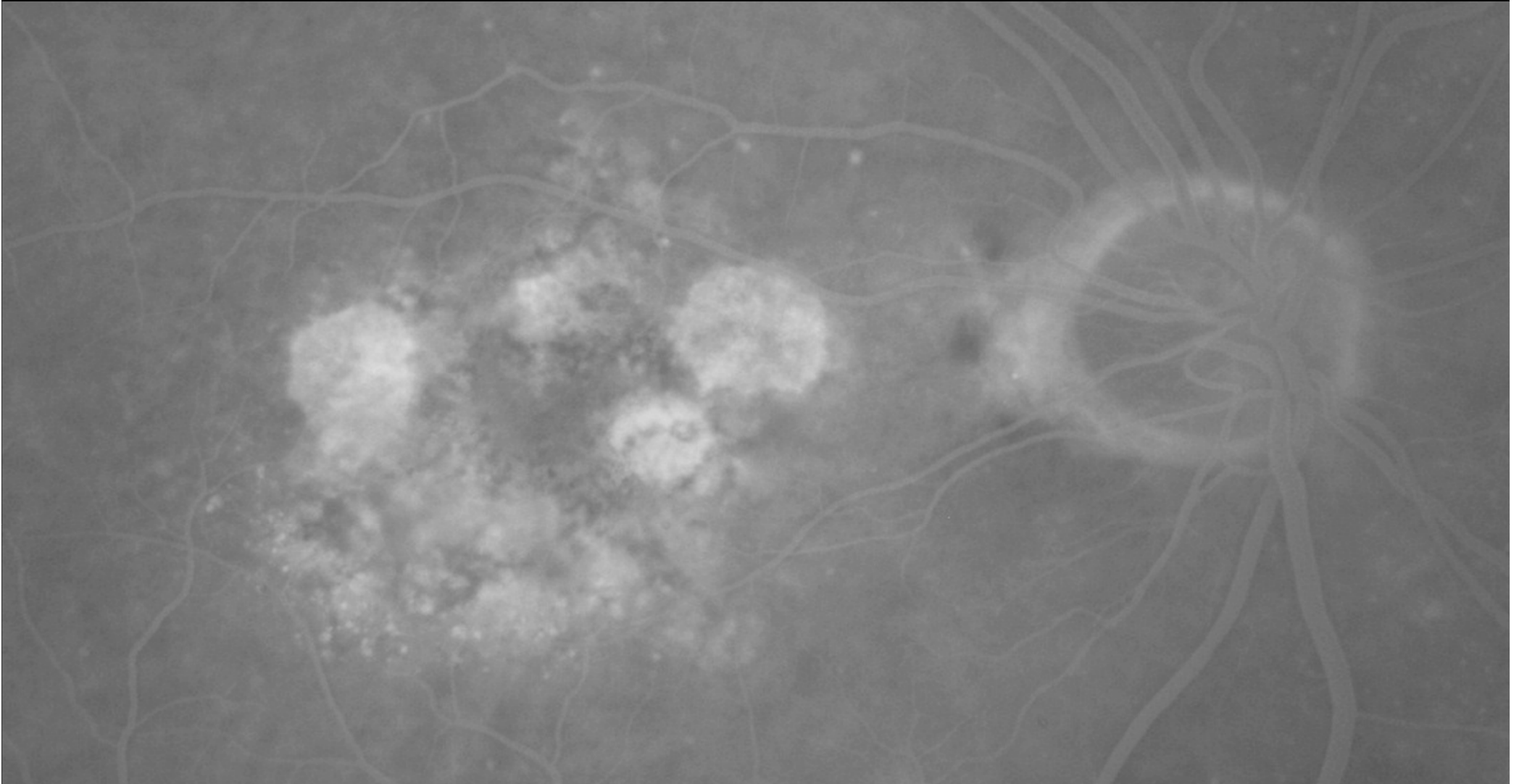
- However ...

- Not always performed
- Limitations for interpretation

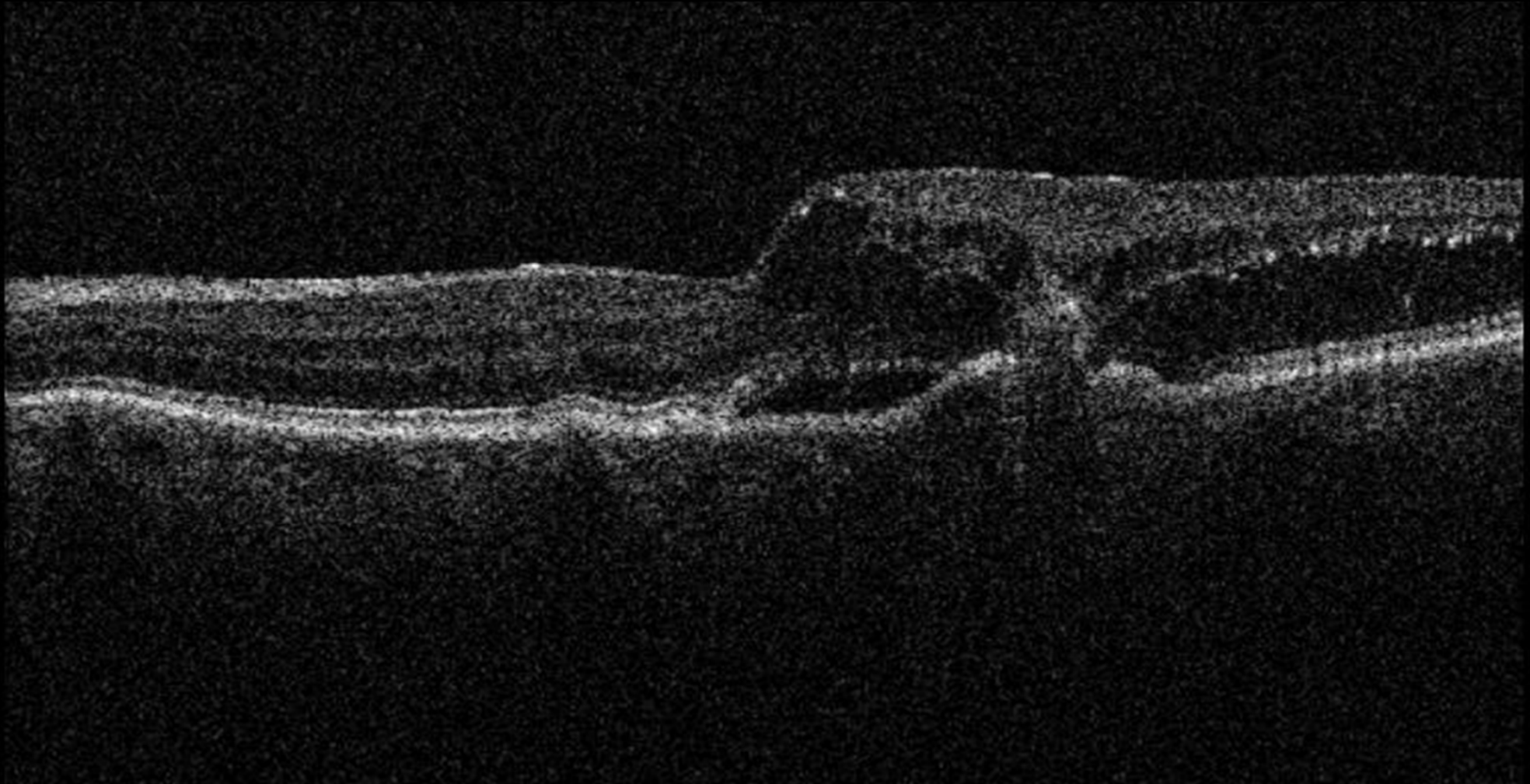
RESISTANT NEOVASCULAR AMD

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



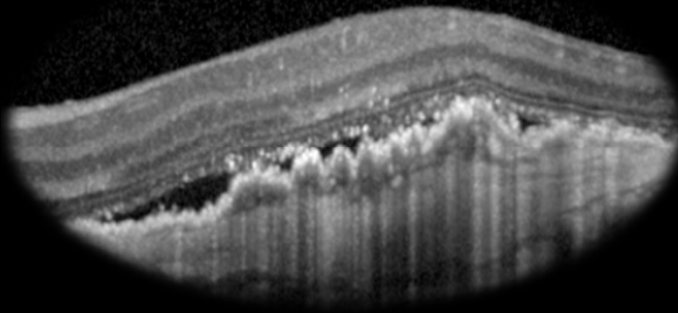
AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



TYPE 1 CNV



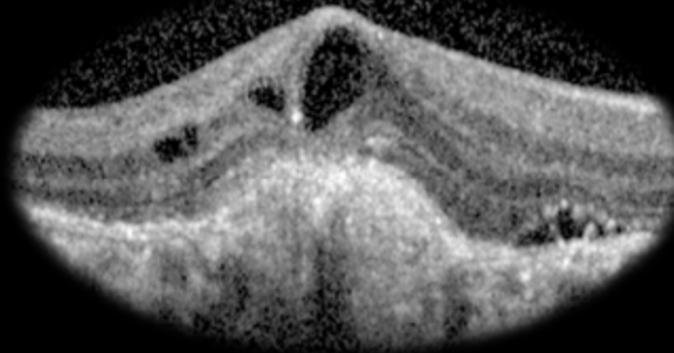
UNDER THE RPE

SUBRETINAL FLUID

EZ & ELM INTACT

RPE INTACT

TYPE 2 CNV



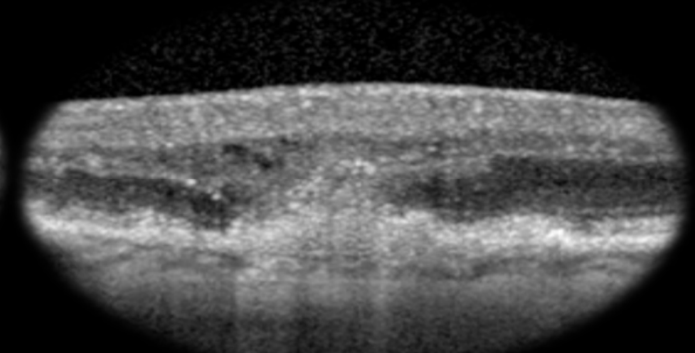
ABOVE THE RPE

INTRARETINAL FLUID

LOSS OF EZ & ELM

RPE DISRUPTED

TYPE 3 CNV



INTRARETINAL

INTRARETINAL FLUID

LOSS OF EZ & ELM

RPE EROSION

Do we need a new classification for choroidal neovascularization in age-related macular degeneration?

K. Bailey Freund KB, Sandrine A. Zweifel, Michael Engelbert



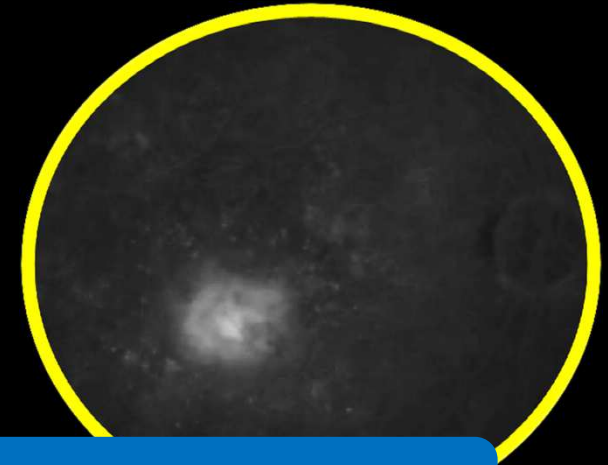
VITREOUS RETINA MACULA
CONSULTANTS OF NEW YORK



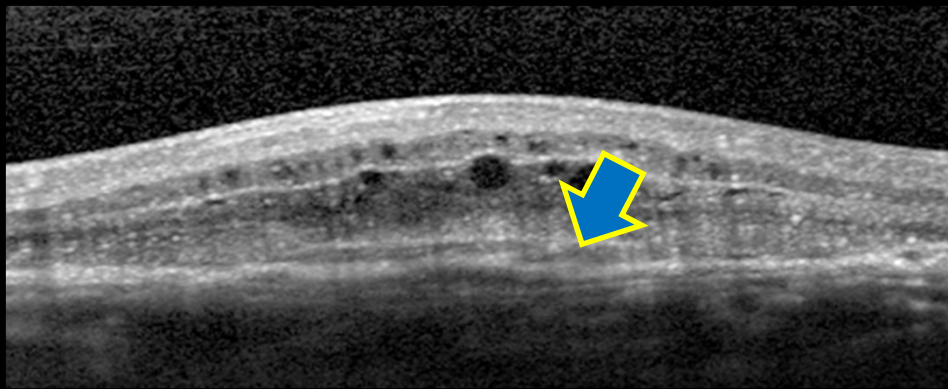
NYU Medical Center / School of Medicine
Department of Ophthalmology

THE MACULA FOUNDATION
EXPANDING THE FIELD OF VISION

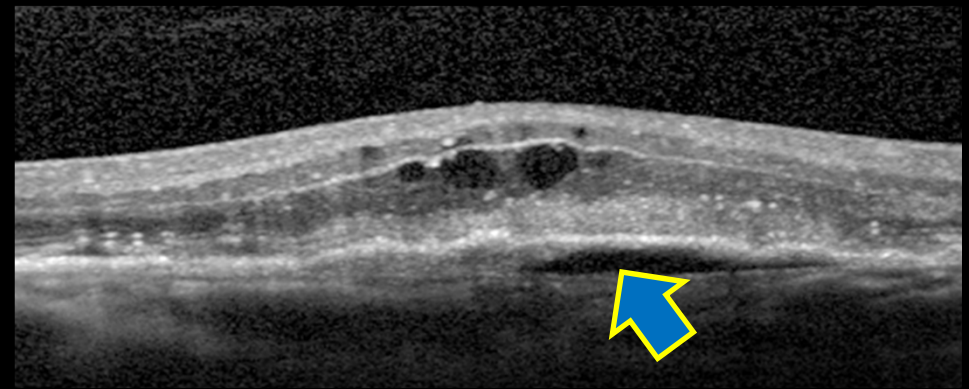
AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



CLASSIC NEOVASCULARIZATION

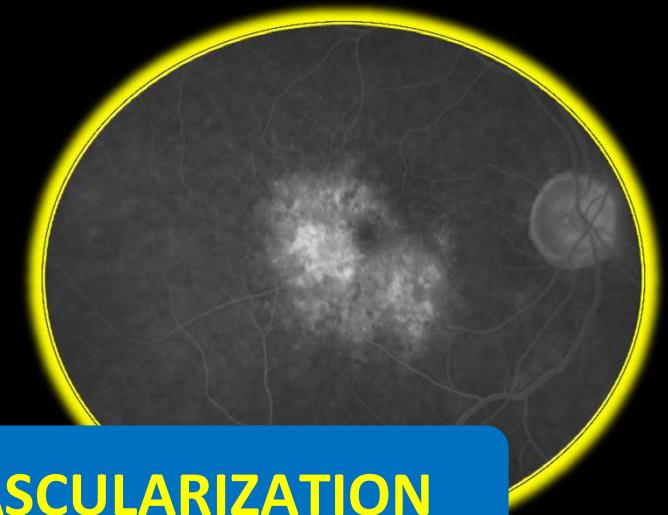
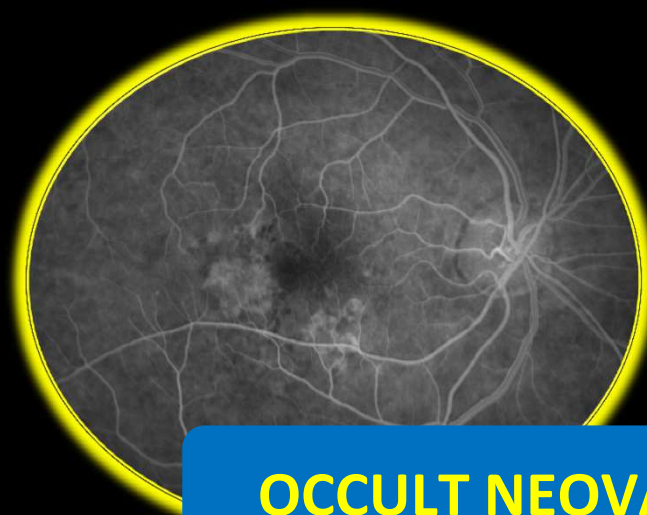
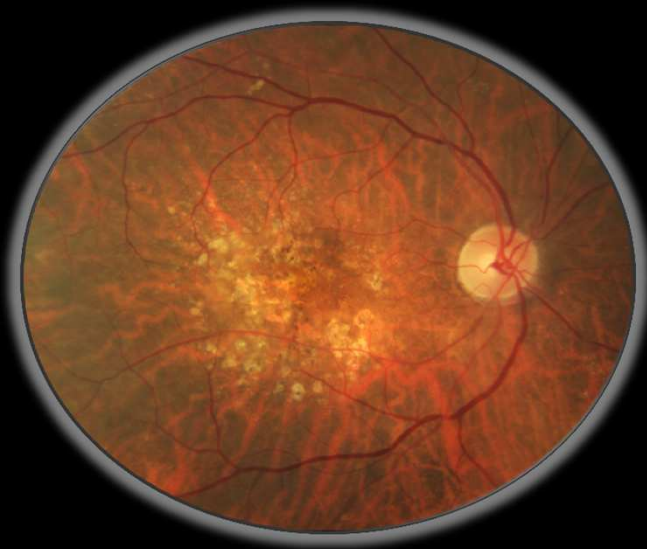


TYPE 2 NEOVASCULARIZATION

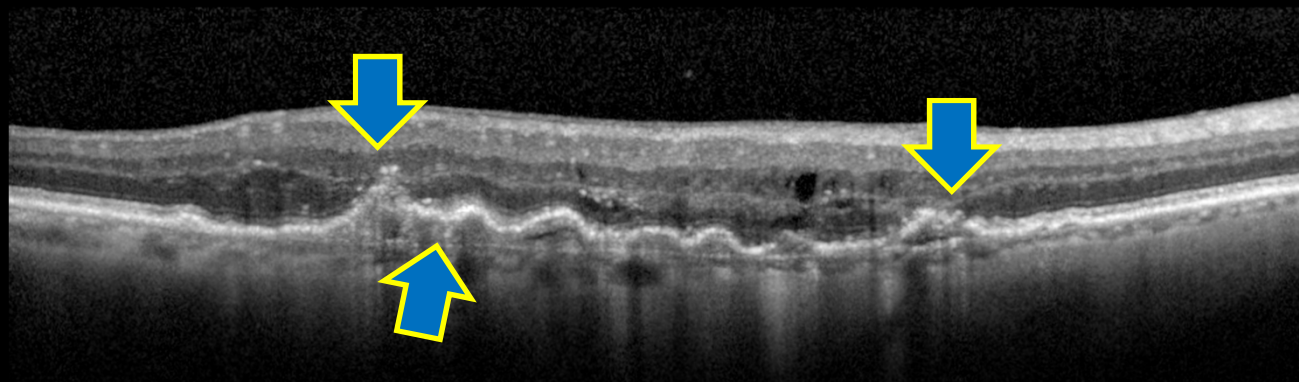


TYPE 1 NEOVASCULARIZATION

AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



OCCULT NEOVASCULARIZATION



TYPE 3 NEOVASCULARIZATION

TYPE 1 NEOVASCULARIZATION

AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



Lesion Type FA alone	Frequency: N=Number (%)	Lesion Type Anatomical (FA + OCT)	Frequency: N=Number (%)
Poorly defined (Occult)	132 (49.6%)	Type 1 (sub-RPE)	106 (39.9%)
Well-defined (Classic)	32 (12.0%)	Type 2 (sub-retinal)	24 (9.0%)
Retinal angiomatous proliferation (RAP)	76 (28.6%)	Type 3 (intraretinal)	91 (34.2%)
Mixed	26 (9.8%)	Mixed	45 (16.9%)

The Incidence of Neovascular Subtypes in Newly Diagnosed Neovascular Age-Related Macular Degeneration

Jesse J. Jung, Christine Y. Chen, Sarah Mrejen, Roberto Gallego-Pinazo, Luna Xu, Marcela Marsiglia, Sucharita Boddur, K. Bailey Freund



VITREOUS RETINA MACULA
CONSULTANTS OF NEW YORK



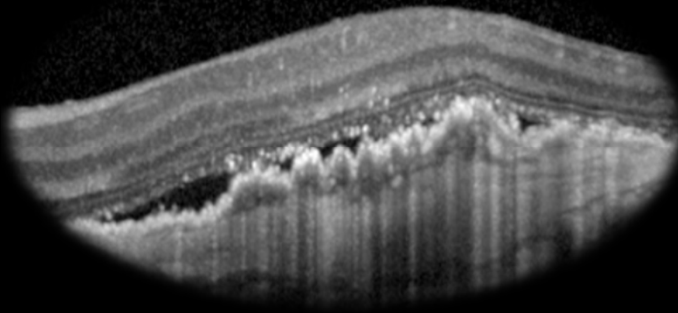
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AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES



TYPE 1 CNV

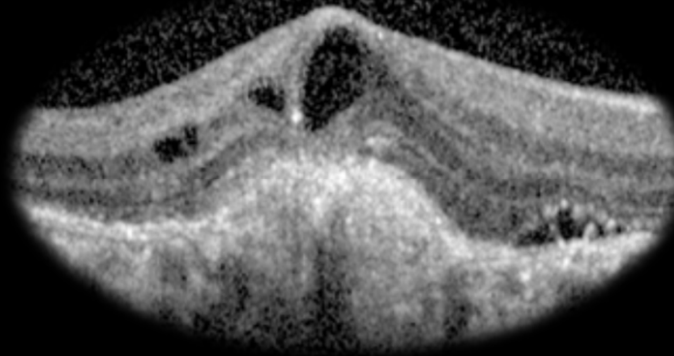


LESS GA

THICKER CHOROID

LESS SDD

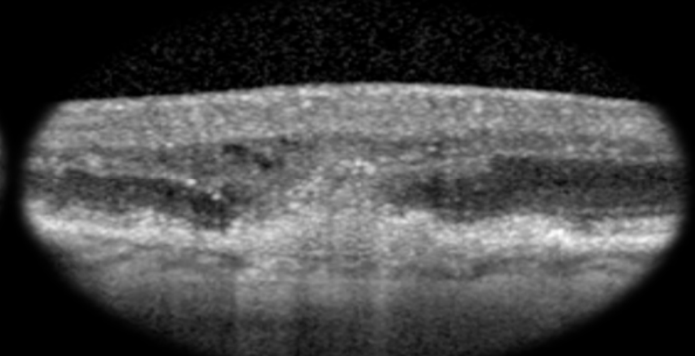
TYPE 2 CNV



MORE GA

PIGMENTATION

TYPE 3 CNV



MORE GA

THINNER CHOROID

MORE SDD

Correlation Between Neovascular Lesion Type and Clinical Characteristics of Non-Neovascular Fellow Eyes in Patients With Unilateral Neovascular Age-Related Macular Degeneration

Sucharita Boddu, Marcela Marsiglia, Christine Y. Chen, Jesse J. Jung, Sarah Mrejen, Roberto Gallego-Pinazo, K. Bailey Freund



VITREOUS RETINA MACULA
CONSULTANTS OF NEW YORK



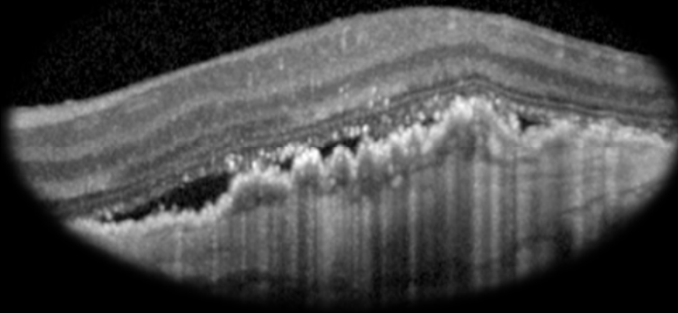
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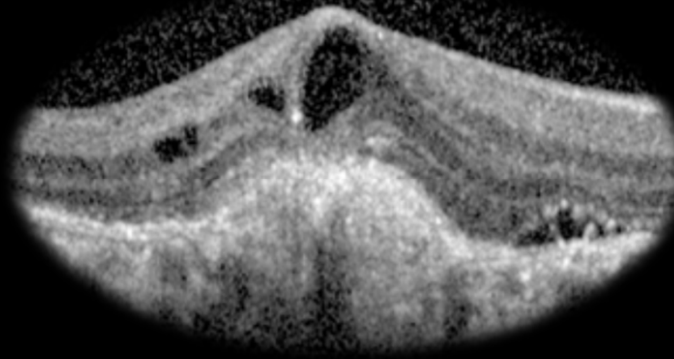


TYPE 1 CNV



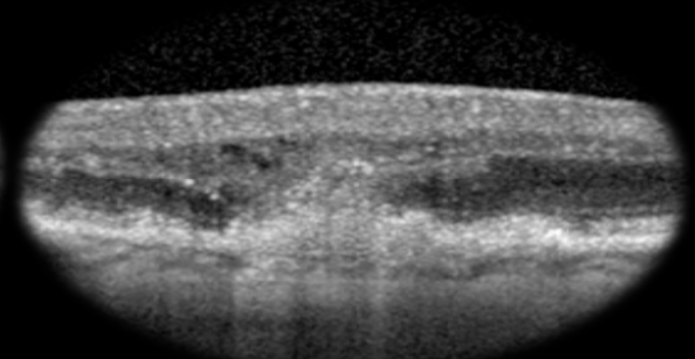
*PRO RE
NATA*

TYPE 2 CNV



*TREAT and
EXTEND*

TYPE 3 CNV



*PRO RE
NATA*

CASES OF UNILATERAL INVOLVEMENT

*TREAT and
EXTEND*

*TREAT and
EXTEND*

*TREAT and
EXTEND*

CASES OF BILATERAL INVOLVEMENT

AMD MANAGEMENT ...

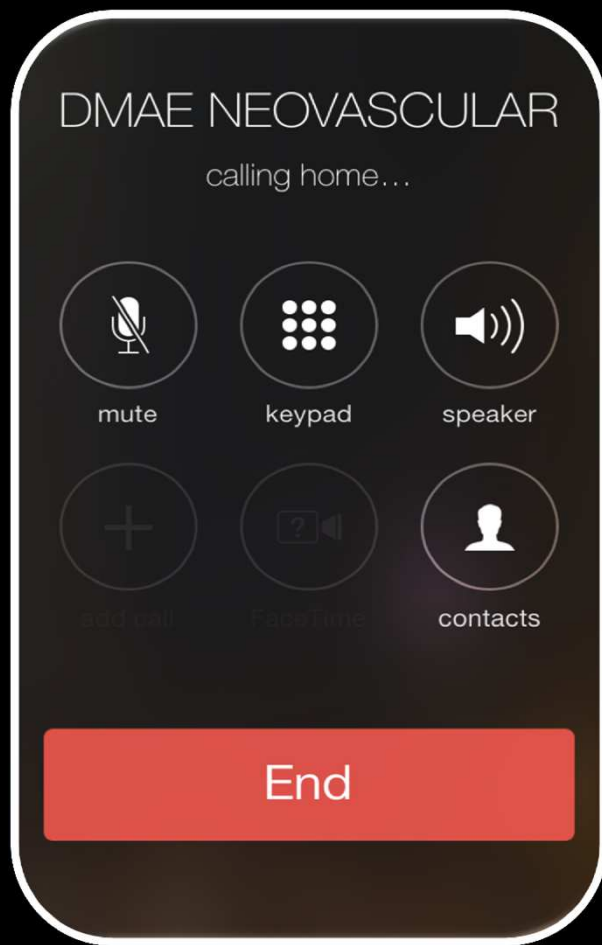
What changes with a new player



AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES

IDENTIFICATION AND MANAGEMENT OF RESISTANT NEOVASCULAR AMD

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

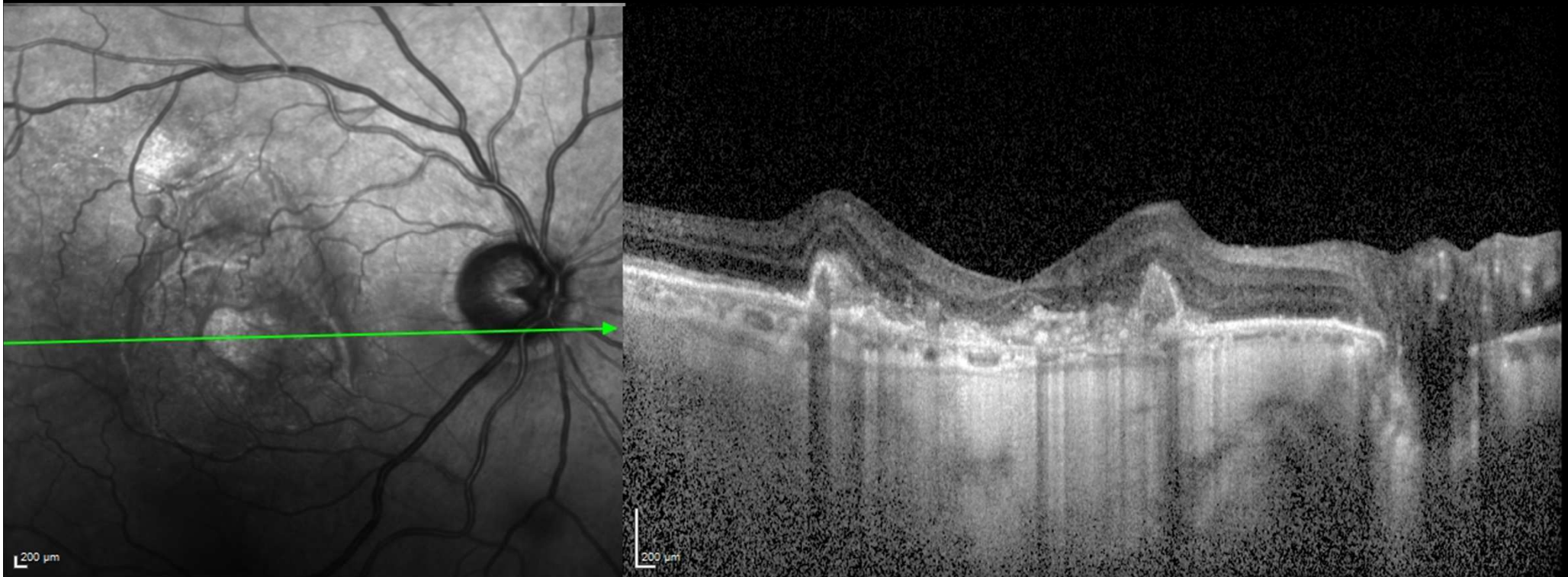


WRONG NUMBER
MISDIAGNOSIS

NO COVERAGE
ANATOMIC DISTORTION

PHONE BUSY
REAL NON-RESPONDER

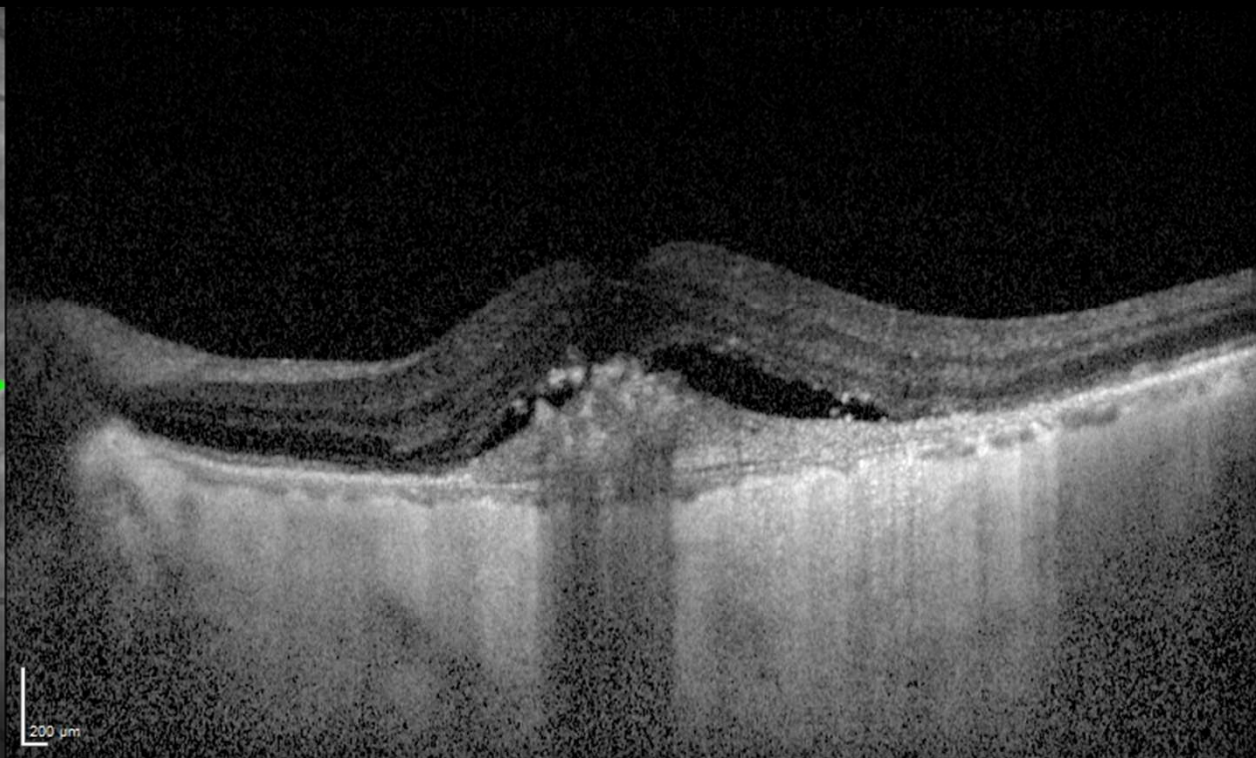
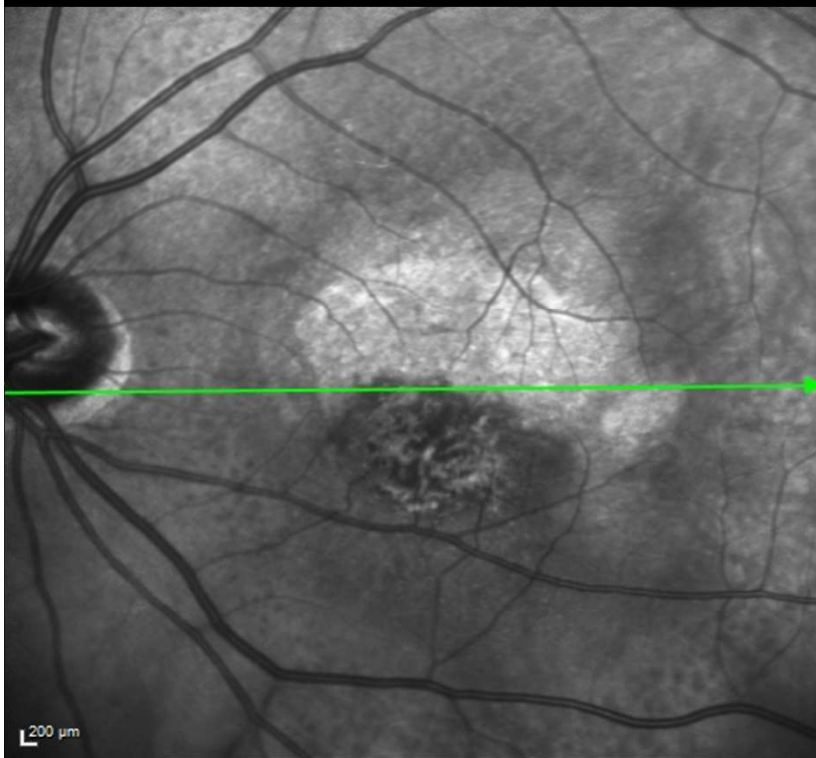
NO COVERAGE *ANATOMIC DISTORTION*



24/10/2013, OD

IR&OCT 30° EDI 5566.12 [HS] ART(16) Q: 18

NO COVERAGE *ANATOMIC DISTORTION*



04/02/2014, OS

IR&OCT 30° EDI 9754.18 [HS] ART(16) Q: 19

STRATEGIES FOR THE MANAGEMENT OF RESISTANT NEOVASCULAR AMD

1

CONFIRM PRECISE DIAGNOSIS OF NEOVASCULAR AMD

2

CONFIRM REAL PATTERN OF THERAPEUTIC RESPONSE

3

CHANGE THERAPEUTIC STRATEGY PERFORMED

Roberto Gallego-Pinazo

Unit of Macula, Department of Ophthalmology
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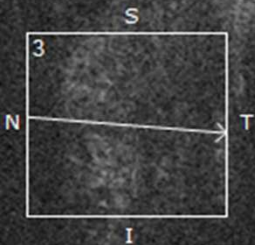
Roberto Gallego-Pinazo

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1

CONFIRM PRECISE DIAGNOSIS OF NEOVASCULAR AMD

ACQUIRED VITELLIFORM LESION



1

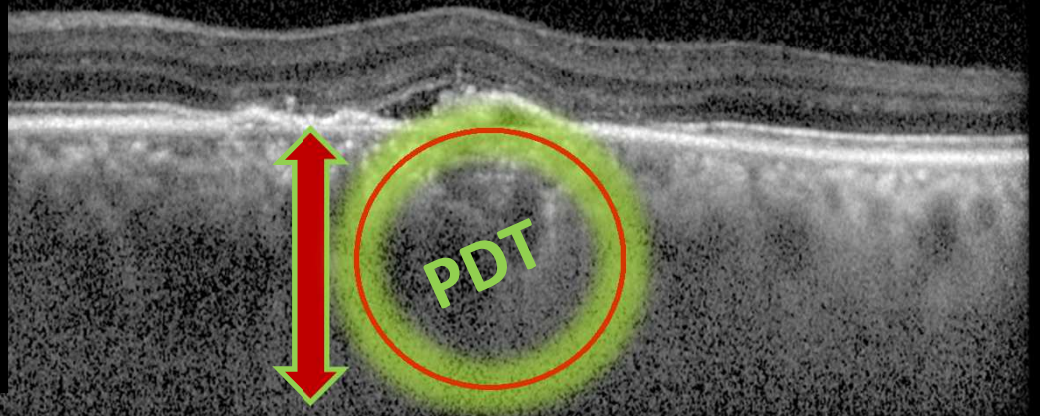
CONFIRM PRECISE DIAGNOSIS OF NEOVASCULAR AMD

PACHYCHOROID PIGMENT EPITHELIOPATHY

DAVID J. WARROW, MD,* QUAN V. HOANG, MD, PhD,†‡§ BAILEY K. FREUND, MD†‡§¶

TYPE 1 (SUB-RETINAL PIGMENT EPITHELIAL) NEOVASCULARIZATION IN CENTRAL SEROUS CHORIORETINOPATHY MASQUERADING AS NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

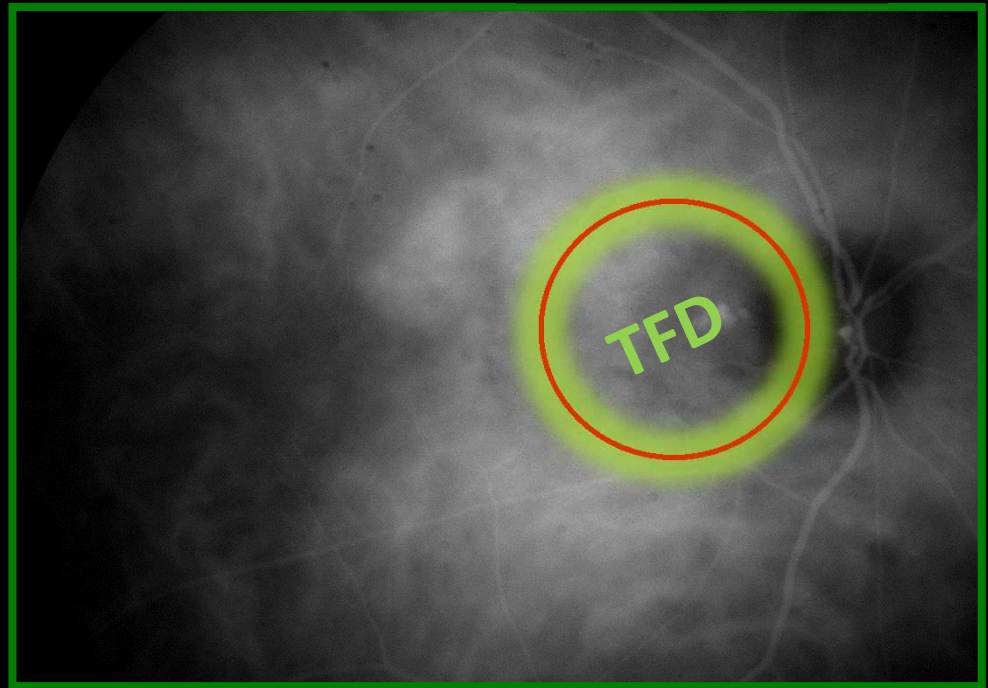
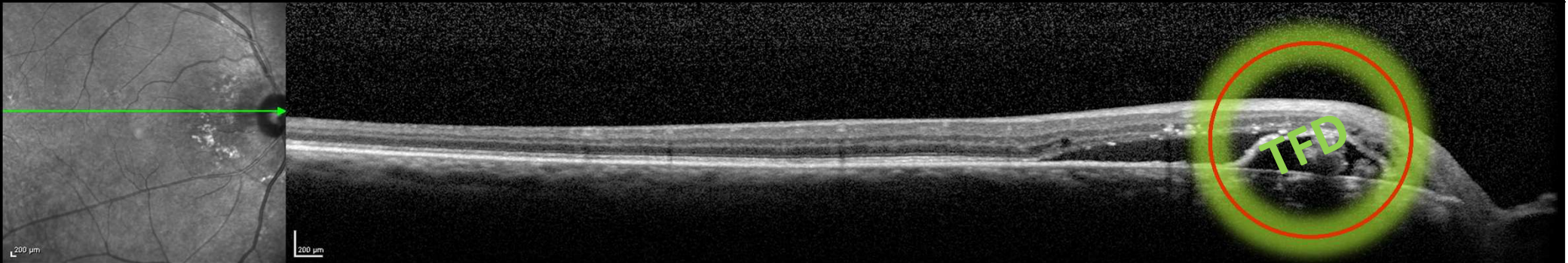
ADRIAN T. FUNG, MBBS, MMed,* LAWRENCE A. YANNUZZI, MD,*†‡
K. BAILEY FREUND, MD*†‡



PACHYCHOROID NEOVASCULOPATHY

1

CONFIRM PRECISE DIAGNOSIS OF NEOVASCULAR AMD



Dr LA Yannuzzi & KB Freund

STRATEGIES FOR THE MANAGEMENT OF RESISTANT NEOVASCULAR AMD

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2

CONFIRM REAL PATTERN OF THERAPEUTIC RESPONSE

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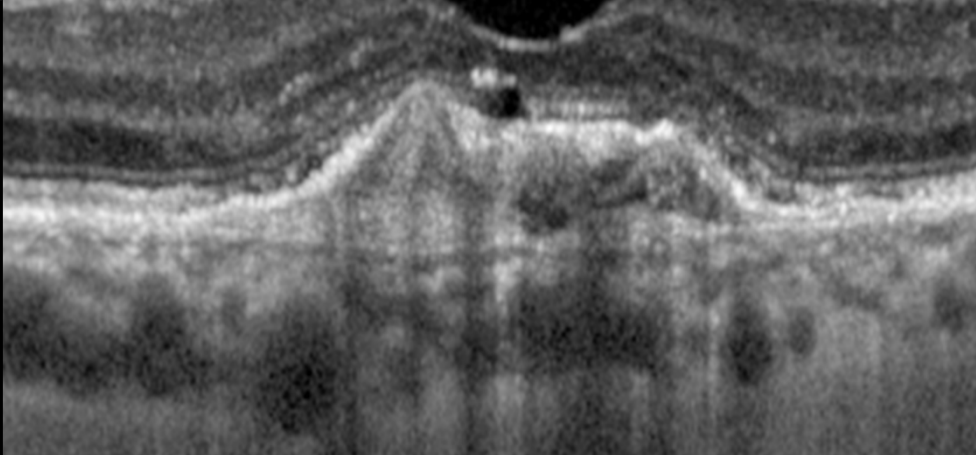
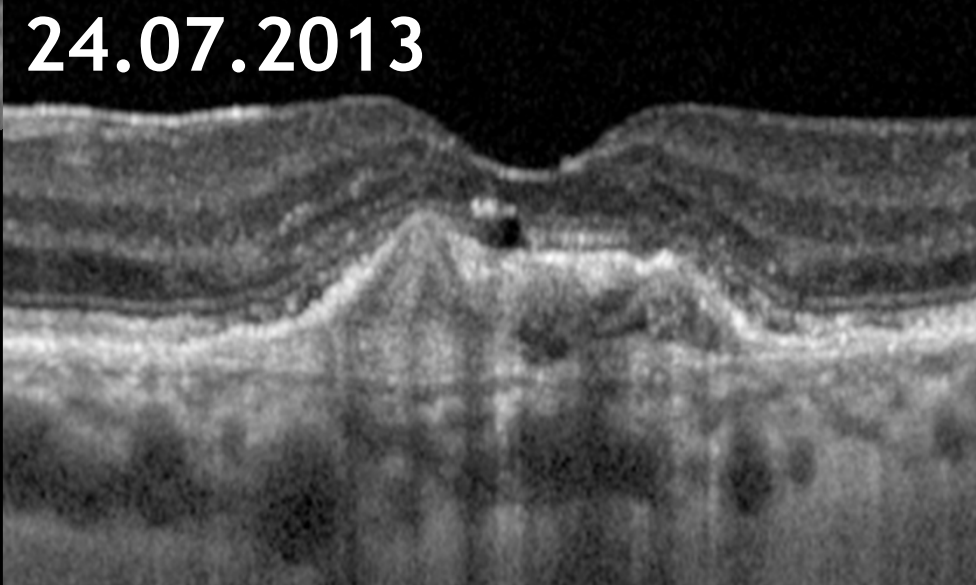
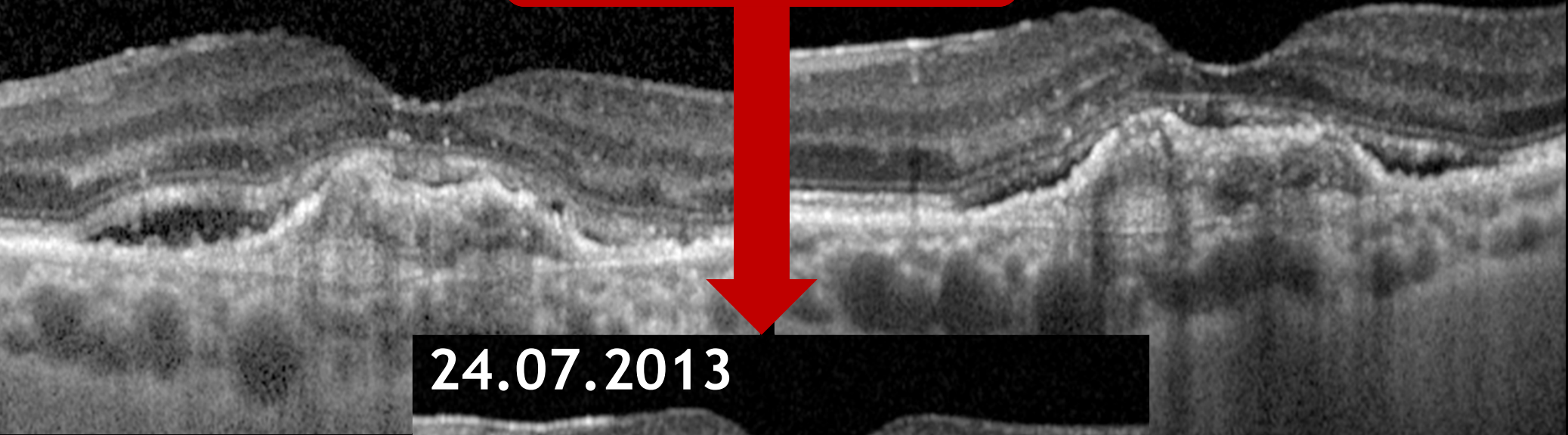
2

CONFIRM REAL PATTERN OF THERAPEUTIC RESPONSE

26.06.2013

4 WEEKS

14.08.2013



STRATEGIES FOR THE MANAGEMENT OF RESISTANT NEOVASCULAR AMD

1

CONFIRM PRECISE DIAGNOSIS OF NEOVASCULAR AMD

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CONFIRM REAL PATTERN OF THERAPEUTIC RESPONSE

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CHANGE THERAPEUTIC STRATEGY PERFORMED

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3

CHANGE THERAPEUTIC STRATEGY PERFORMED

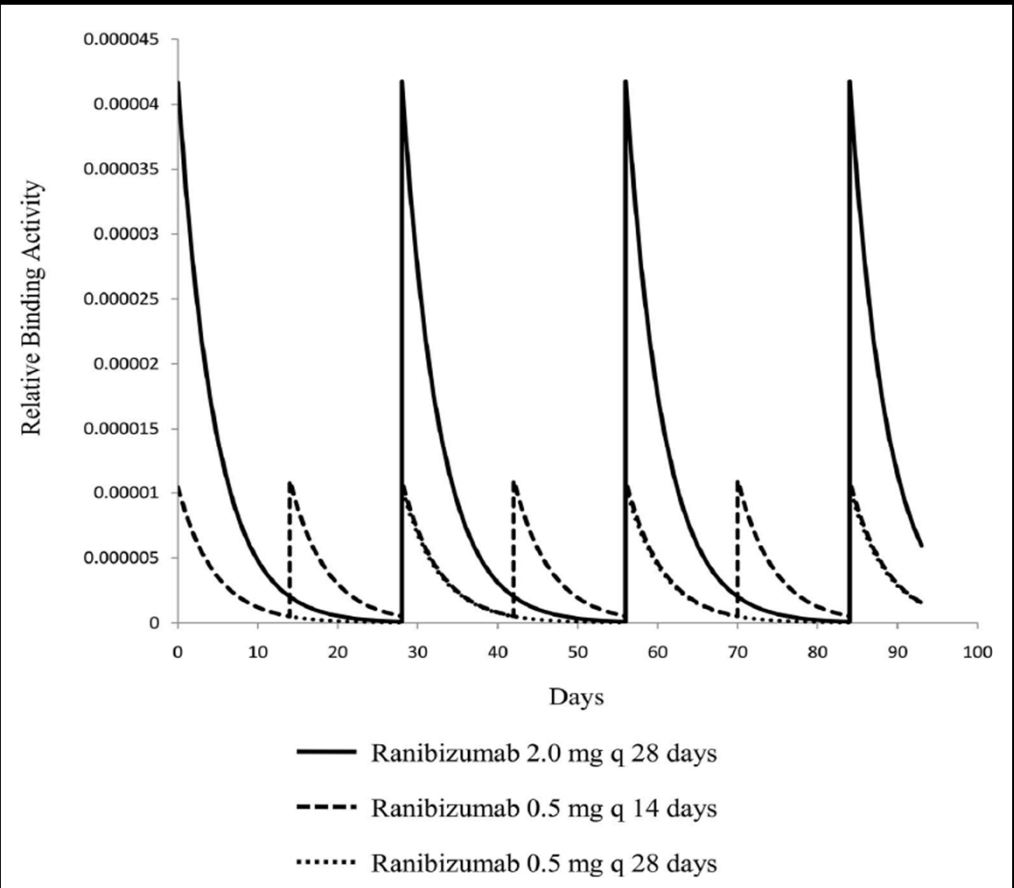
- **Decrease retreatment intervals**
- **Increase antiangiogenic dose**
- **Switch antiangiogenic agent**

3

CHANGE THERAPEUTIC STRATEGY PERFORMED

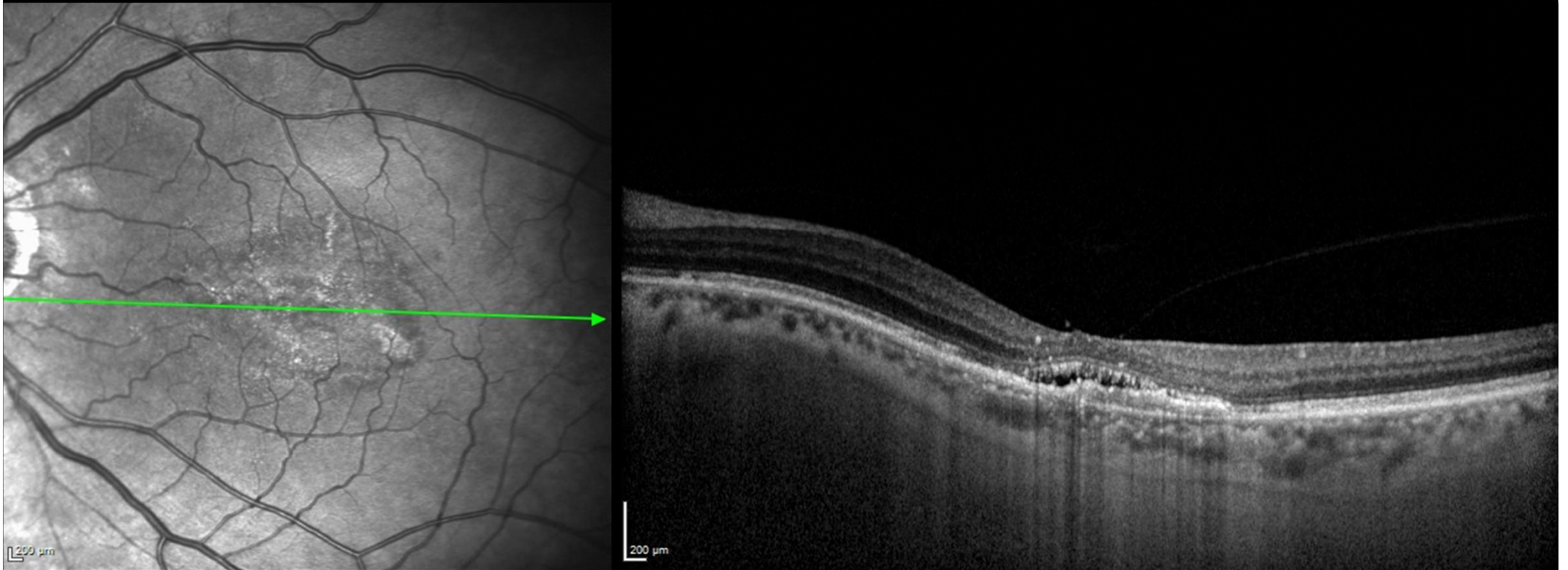
**PHARMACOKINETIC RATIONALE FOR
DOSING EVERY 2 WEEKS VERSUS
4 WEEKS WITH INTRAVITREAL
RANIBIZUMAB, BEVACIZUMAB, AND
AFLIBERCEPT (VASCULAR ENDOTHELIAL
GROWTH FACTOR TRAP-EYE)**

MICHAEL W. STEWART, MD,* PHILIP J. ROSENFELD, MD, PhD,† FERNANDO M. PENHA, MD, PhD,†
FENGHUA WANG, MD,†‡ ZOHAR YEHOSSUA, MD, MHA,† ELENA BUENO-LOPEZ, MD,§¶
PEDRO F. LOPEZ, MD§¶



3

CHANGE THERAPEUTIC STRATEGY PERFORMED



3

CHANGE THERAPEUTIC STRATEGY PERFORMED

- Decrease retreatment intervals
- Increase antiangiogenic dose
- Switch antiangiogenic agent

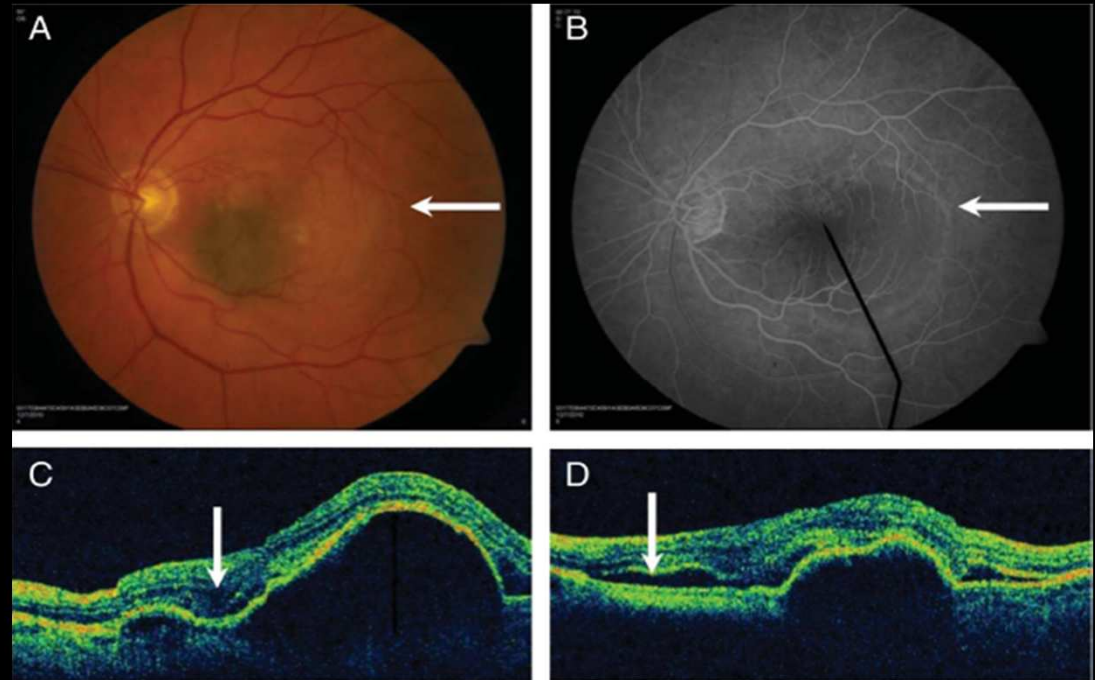
3

CHANGE THERAPEUTIC STRATEGY PERFORMED

PROSPECTIVE EVALUATION OF THE INCIDENCE AND RISK FACTORS FOR THE DEVELOPMENT OF RPE TEARS AFTER HIGH- AND LOW-DOSE RANIBIZUMAB THERAPY

DAVID SARRAF, MD,*† CLEMENT CHAN, MD,‡§ EHSAN RAHIMY, MD,* PREMA ABRAHAM, MD¶

retinal degeneration in patients with persistent/recurrent macular fluid <30 days following treatment with intravitreal anti-VEGF therapy (the LAST Study)



2.0mg R
SHOWS EFFIC

3

CHANGE THERAPEUTIC STRATEGY PERFORMED

- Decrease retreatment intervals
- Increase antiangiogenic dose
- **Switch antiangiogenic agent**

3

CHANGE THERAPEUTIC STRATEGY PERFORMED

(OBVIOUSLY) SWITCHING DRUGS MAY ACHIEVE POSITIVE OUTCOMES IN SOME RESISTANT NEOVASCULAR AMD PATIENTS

A

VERIFY LACK OF ANATOMIC RESPONSE TO THERAPY

B

PERFORM THE SWAP AFTER INJECTION #6

C

INITIATE NEW TREATMENT WITH 3 MONTHLY INJECTIONS

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AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



1

TREATMENT-NAÏVE CASES OF NEOVASCULAR AMD

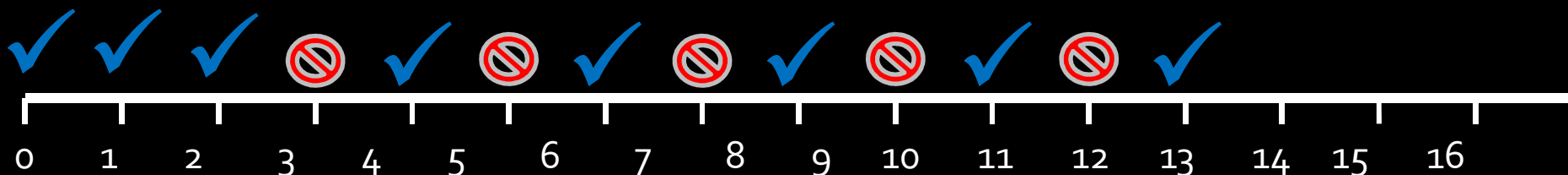
2

RESISTANT CASES OF NEOVASCULAR AMD

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

PROS

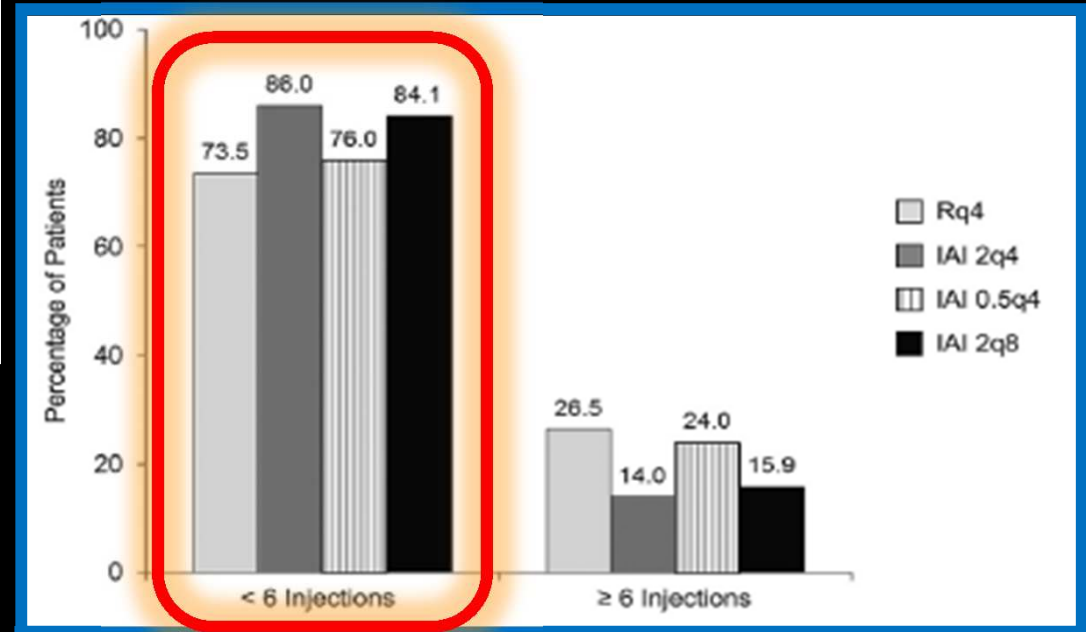
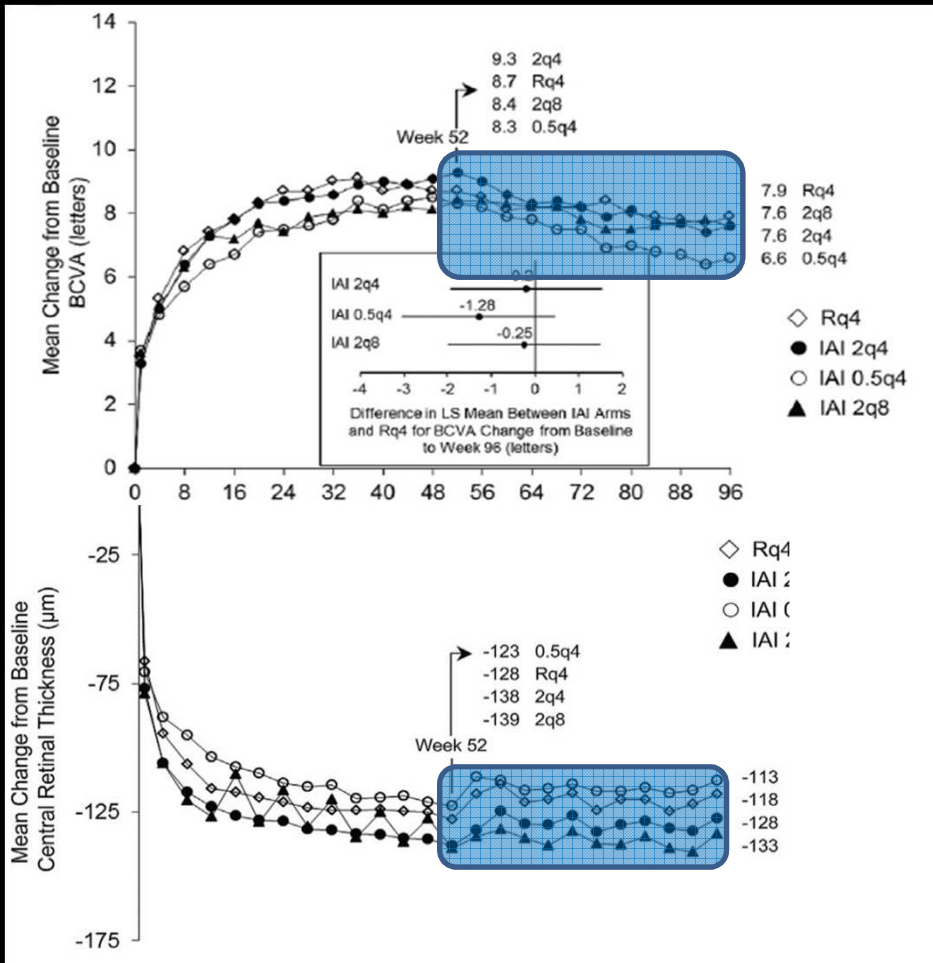
- LESS NUMBER OF VISITS
- LESS NUMBER OF TREATMENTS
- MORE “DRY RETINA”



CONS

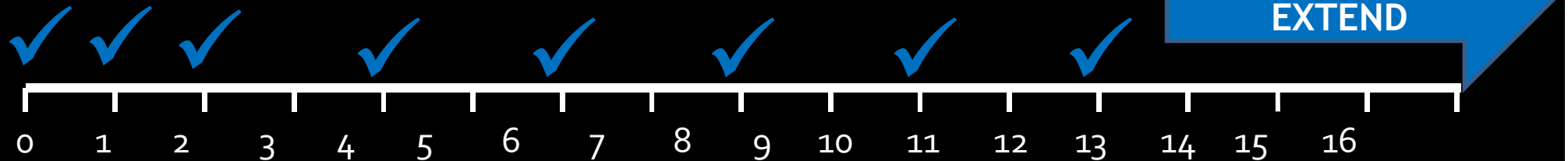
- MORE GEOGRAPHIC ATROPHY (?)
- SAW-TOOTH PATTERN OF RETINAL THICKNESS (?)
- SYSTEMIC SAFETY ISSUES (?)

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



**>40% OF CASES ONLY
NEEDED THE FIXED
TRI-MONTHLY INJECTIONS**

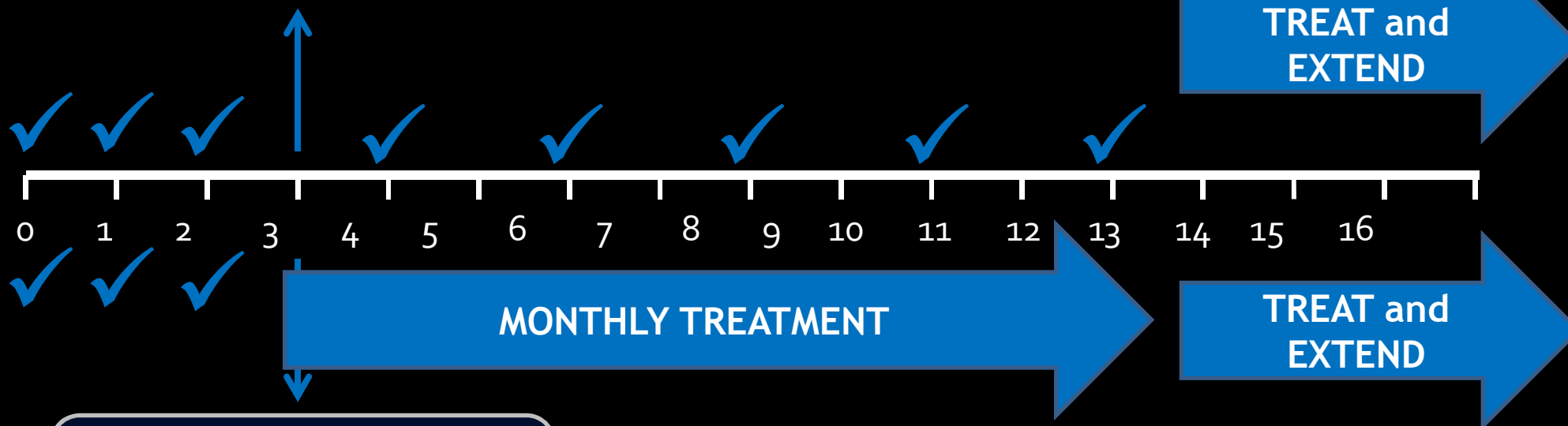
AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



FLUID RESOLUTION
[~80%]



PERSISTENT FLUID
[~20%]

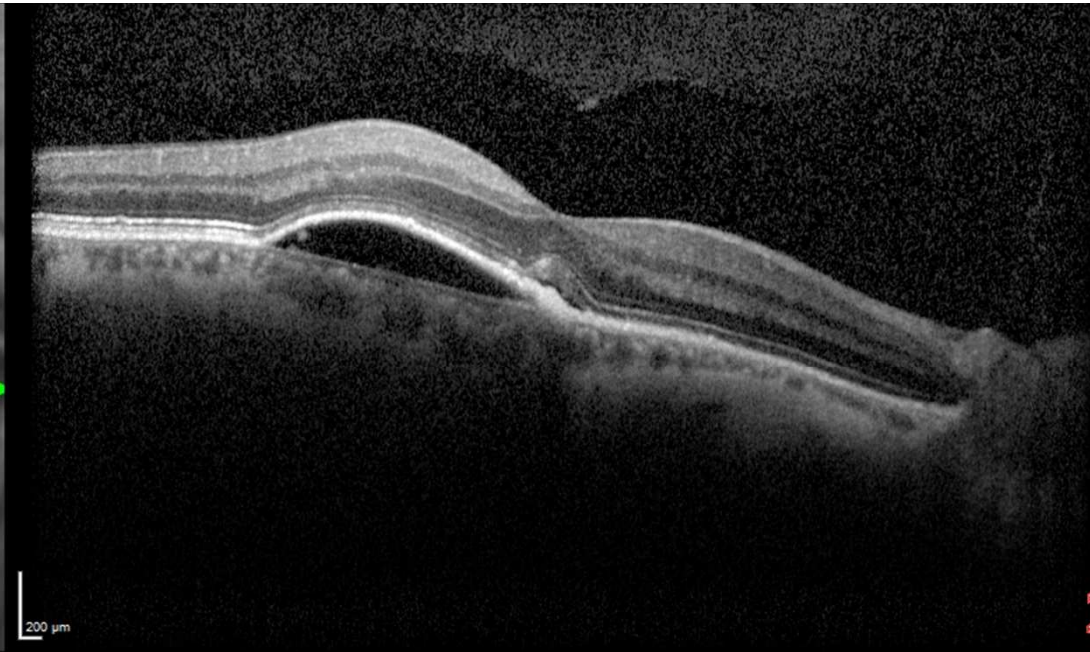
AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



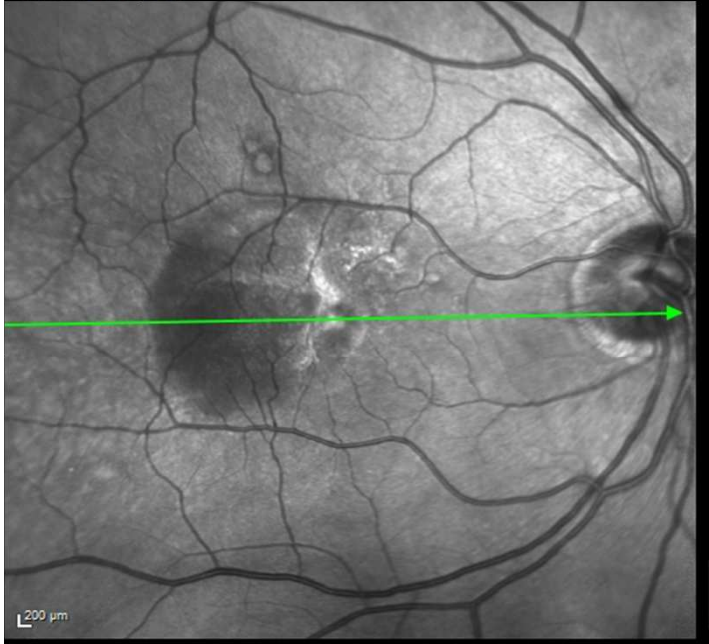
- **IDEAL CANDIDATES FOR FIRST LINE THERAPY WITH EYLEA**
 - Type 1 neovascularization
 - Large serous/vascularized PED
 - Thick choroidal tissue
 - Limitations for multiple visits



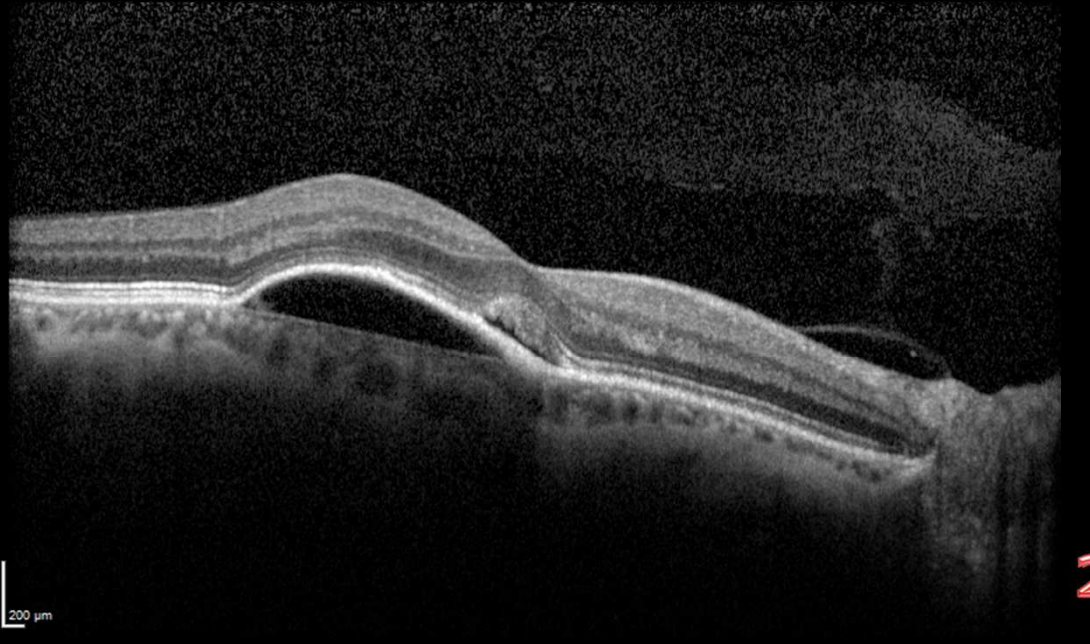
12/02/2014, OD



20/35
LUCENTIS[®] 21



08/01/2014, OD



20/30
EYLEA[®] 3



Patient disposition (all randomized subjects):

Study VIEW 1	RQ4	2Q4	0.5Q4	2Q8	VEGF Trap-Eye Combined	Total
Screened*						2063
Randomized	306 (100)	304 (100)	304 (100)	303 (100)	911 (100)	1217 (100)
Treated ² (safety set)	304 (99.3)	304 (100)	304 (100)	303 (100)	911 (100)	1215 (99.8)
FAS ¹	304 (99.3)	304 (100)	301 (99.0)	301 (99.3)	906	1210
PPS	269 (87.9)	285 (93.8)	270 (88.8)	265 (87.5)	820	1089
Completed Year 1	284 (92.8)	293 (96.4)	277 (91.1)	276 (91.1)	846 (92.9)	1130 (92.9)
Premature discontinuation within first year						
Total	22 (7.2)	11 (3.6)	27 (8.9)	27 (8.9)	65 (7.1)	87 (7.1)
Subject withdrawal	10 (3.3)	5 (1.6)	7 (2.3)	8 (2.6)	20 (2.2)	30 (2.5)
Adverse event	4 (1.3)	3 (1.0)	5 (1.6)	4 (1.3)	12 (1.3)	16 (1.3)
Death*	3 (1.0)	1 (0.3)	2 (0.7)	7 (2.3)	10 (1.1)	13 (1.1)
Lost to follow-up	1 (0.3)	2 (0.7)	4 (1.3)	4 (1.3)	10 (1.1)	11 (0.9)
Protocol deviation*	3 (1.0)	0	3 (1.0)	1 (0.3)	4 (0.4)	7 (0.6)
Treatment failure	0	0	2 (0.7)	2 (0.7)	4 (0.4)	4 (0.3)
Other	1 (0.3)	0	4 (1.3)	1 (0.3)	5 (0.5)	6 (0.5)
Completed study medication	279 (91.2)	288 (94.7)	274 (90.1)	273 (90.1)	911 (100)	1114 (91.5)
Prematurely discontinued study medication	27 (8.8)	16 (5.3)	30 (9.9)	30 (9.9)	76 (8.3)	103 (8.5)
Withdrawal by Subject	12 (3.9)	8 (2.6)	9 (3.0)	9 (3.0)	—	38 (3.1)
Adverse event	4 (1.3)	3 (1.0)	5 (1.6)	6 (2.0)	14 (1.5)	18 (1.5)
Lost to follow-up	2 (0.7)	4 (1.3)	4 (1.3)	5 (1.7)	13 (1.4)	15 (1.2)
Death	3 (1.0)	1 (0.3)	2 (0.7)	6 (2.0)	9 (1.0)	12 (1.0)
Protocol deviation*	3 (1.0)	0 (0.0)	3 (1.0)	1 (0.3)	4 (0.4)	7 (0.6)
Treatment failure	1 (0.3)	0 (0.0)	2 (0.7)	2 (0.7)	4 (0.4)	5 (0.4)
Other	2 (0.7)	0 (0.0)	5 (1.6)	1 (0.3)	6 (0.7)	8 (0.7)



Table 3: Number of subjects with non-ocular treatment-emergent adverse event in the elderly population grouped by age (Year 1 data)

Age Group	< 65 years		≥ 65 – < 75 years		≥ 75 – < 85 years		≥ 85 years	
	Ranibizumab N=71 (100%)	VEGF Trap- Eye (Total) N=202 (100%)	Ranibizumab N=163 (100%)	VEGF Trap- Eye (Total) N=478 (100%)	Ranibizumab (N=274 (100%))	VEGF Trap- Eye (Total) N=861 (100%)	Ranibizumab N=274 (100%)	VEGF Trap- Eye (Total) N=861 (100%)
Any non-ocular TEAEs	43 (60.6%)	144 (71.3%)	105 (64.4%)	335 (70.1%)	200 (73.0%)	623 (72.4%)	67 (77.0%)	222 (78.4%)
Fatal (ie, deaths)	0	0	1 (0.6%)	1 (0.2%)	3 (1.1%)	5 (0.6%)	3 (3.4%)	7 (2.5%)
Serious	1 (1.4%)	15 (7.4%)	19 (11.7%)	48 (10.0%)	44 (16.1%)	117 (13.6%)	19 (21.8%)	72 (25.4%)
Withdrawals or discontinuations	0	4 (2.0%)	1 (0.6%)	6 (1.3%)	3 (1.1%)	14 (1.6%)	1 (1.1%)	9 (3.2%)
Any non-ocular TEAEs by AE grouping								
CNS (confusion/extrapyramidal)	1 (1.4%)	5 (2.5%)	6 (3.7%)	3 (0.6%)	5 (1.8%)	14 (1.6%)	1 (1.1%)	10 (3.5%)
AE related to falling	0	2 (1.0%)	5 (3.1%)	4 (0.8%)	16 (5.8%)	24 (2.8%)	5 (5.7%)	25 (8.8%)
Cardiovascular events	0	6 (3.0%)	1 (0.6%)	12 (2.5%)	11 (4.0%)	26 (3.0%)	8 (9.2%)	8 (2.8%)
Cerebrovascular events	0	0	0	5 (1.0%)	1 (0.4%)	10 (1.2%)	1 (1.1%)	20 (7.1%)
Infections and Infestations	23 (32.4%)	49 (24.3%)	54 (33.1%)	140 (29.3%)	96 (35.0%)	239 (27.8%)	27 (31.0%)	86 (30.4%)



Table 7: Number of subjects with non-ocular treatment-emergent adverse event in the elderly population grouped by age (2 Year data)

Age Group	< 65 years		≥ 65 – < 75 years		≥ 75 – < 85 years		≥ 85 years	
	Ranibizumab N= 71 (100%)	VEGF Trap- Eye (Total) N=202(100%)	Ranibizumab N= 163(100%)	VEGF Trap- Eye (Total) N= 478 (100%)	Ranibizumab (N= 274 (100%)	VEGF Trap-Eye (Total) N= 861(100%)	Ranibizumab N= 87 (100%)	VEGF Trap-Eye (Total) N= 283 (100%)
Any non-ocular TEAEs	51 (71.8%)	166 (82.2%)	129 (79.1%)	393 (82.2%)	235 (85.8%)	732 (85.0%)	79 (90.8%)	251 (88.7%)
Fatal ie, deaths	0	1 (0.5%)	2 (1.2%)	8 (1.7%)	6 (2.2%)	20 (2.3%)	7 (8.0%)	17 (6.0%)
Serious	5 (7.0%)	21 (10.4%)	29 (17.8%)	83 (17.4%)	80 (29.2%)	221 (25.7%)	32 (36.8%)	112 (39.6%)
Withdrawals or discontinuations	0	5 (2.5%)	2 (1.2%)	11 (2.3%)	7 (2.6%)	32 (3.7%)	4 (4.6%)	25 (8.8%)
Any non-ocular TEAEs by AE grouping								
CNS (confusion/extrapyramidal)	2 (2.8%)	8 (4.0%)	9 (5.5%)	8 (1.7%)	9 (3.3%)	26 (3.0%)	2 (2.3%)	15 (5.3%)
AE related to falling	0	6 (3.0%)	6 (3.7%)	8 (1.7%)	24 (8.8%)	49 (5.7%)	9 (10.3%)	47 (16.6%)
Cardiovascular events	3 (4.2%)	6 (3.0%)	8 (4.9%)	21 (4.4%)	18 (6.6%)	41 (4.8%)	9 (10.3%)	21 (7.4%)
Cerebrovascular events	0	2 (1.0%)	0	6 (1.3%)	9 (3.3%)	20 (2.3%)	3 (3.4%)	27 (9.5%)
Infections and Infestations	28 (39.4%)	63 (31.2%)	70 (42.9%)	182 (38.1%)	134 (48.9%)	360 (41.8%)	40 (46.0%)	123 (43.5%)
AFTC events	1 (1.4%)	2 (1.0%)	2 (1.2%)	11 (2.3%)	11 (4.0%)	24 (2.8%)	5 (5.7%)	23 (8.1%)

Table 3: Number of subjects with non-ocular treatment-emergent adverse event in the elderly population grouped by age (Year 1 data)

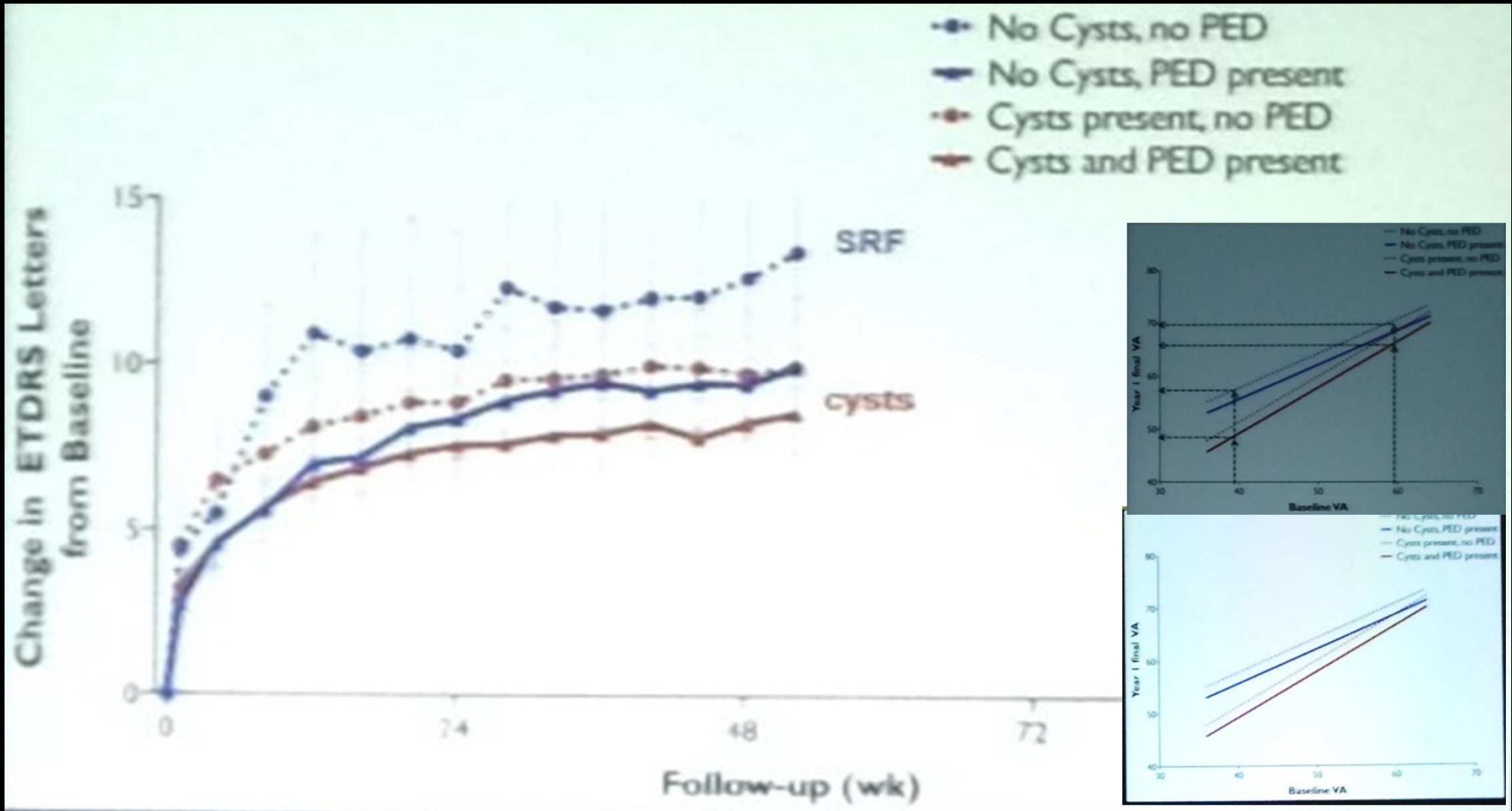
Age Group	< 65 years		≥ 65 – < 75 years		≥ 75 – < 85 years		≥ 85 years	
	Ranibizumab N=71 (100%)	VEGF Trap- Eye (Total) N=202 (100%)	Ranibizumab N=163 (100%)	VEGF Trap- Eye (Total) N=478 (100%)	Ranibizumab (N=274 (100%))	VEGF Trap- Eye (Total) N=861 (100%)	Ranibizumab N=274 (100%)	VEGF Trap- Eye (Total) N=861 (100%)
Any non-ocular TEAEs	43 (60.6%)	144 (71.3%)	105 (64.4%)	335 (70.1%)	200 (73.0%)	623 (72.4%)	67 (77.0%)	222 (78.4%)
Fatal (ie, deaths)	0	0	1 (0.6%)	1 (0.2%)	3 (1.1%)	5 (0.6%)	3 (3.4%)	7 (2.5%)
Serious	1 (1.4%)	15 (7.4%)	19 (11.7%)	48 (10.0%)	44 (16.1%)	117 (13.6%)	19 (21.8%)	72 (25.4%)
Withdrawals or discontinuations	0	4 (2.0%)	1 (0.6%)	6 (1.3%)	3 (1.1%)	14 (1.6%)	1 (1.1%)	9 (3.2%)
Any non-ocular TEAEs by AE grouping								
CNS (confusion/extrapyramidal)	1 (1.4%)	5 (2.5%)	6 (3.7%)	3 (0.6%)	5 (1.8%)	14 (1.6%)	1 (1.1%)	10 (3.5%)
AE related to falling	0	2 (1.0%)	3 (1.8%)	4 (0.8%)	16 (5.8%)	24 (2.8%)	5 (5.7%)	25 (8.8%)
Cardiovascular events	0	3 (1.5%)	1 (0.6%)	12 (2.5%)	11 (4.0%)	20 (2.3%)	8 (9.2%)	8 (2.8%)
Corebrovascular events	0	0	0	5 (1.0%)	1 (0.4%)	10 (1.2%)	1 (1.1%)	20 (7.1%)
Infections and Infestations	25 (35.2%)	49 (24.3%)	64 (33.1%)	146 (29.3%)	96 (35.0%)	199 (23.1%)	27 (31.0%)	86 (30.4%)

Table 7: Number of subjects with non-ocular treatment-emergent adverse event in the elderly population grouped by age (2 Year data)

https://www.google.es/search?sourceid=navclient&aq=&oq=EPAR+EYLEA+LUCENTIS&hl=es&ie=UTF-8&rlz=1T4ADRA_esES482ES482&q=EPAR+EYLEA+LUCENTIS&gs_l=hp...0.0.1.538674.....0.4kgA6pANS2E

	N= 71 (100%)	Eye (Total) N=202(100%)	N= 163(100%)	Eye (Total) N= 478 (100%)	(N= 274 (100%))	(Total) N= 861(100%)	N= 87 (100%)	(Total) N= 283 (100%)
Any non-ocular TEAEs	51 (71.8%)	166 (82.2%)	129 (79.1%)	393 (82.2%)	235 (85.8%)	732 (85.0%)	79 (90.8%)	251 (88.7%)
Fatal ie, deaths	0	1 (0.5%)	2 (1.2%)	8 (1.7%)	6 (2.2%)	20 (2.3%)	7 (8.0%)	17 (6.0%)
Serious	5 (7.0%)	21 (10.4%)	29 (17.8%)	83 (17.4%)	80 (29.2%)	221 (25.7%)	32 (36.8%)	112 (39.6%)
Withdrawals or discontinuations	0	5 (2.5%)	2 (1.2%)	11 (2.3%)	7 (2.6%)	32 (3.7%)	4 (4.6%)	25 (8.8%)
Any non-ocular TEAEs by AE grouping								
CNS (confusion/extrapyramidal)	2 (2.8%)	8 (4.0%)	9 (5.5%)	8 (1.7%)	9 (3.3%)	26 (3.0%)	2 (2.3%)	15 (5.3%)
AE related to falling	0	6 (3.0%)	6 (3.7%)	8 (1.7%)	24 (8.8%)	49 (5.7%)	9 (10.3%)	47 (16.6%)
Cardiovascular events	3 (4.2%)	6 (3.0%)	8 (4.9%)	21 (4.4%)	18 (6.6%)	41 (4.8%)	9 (10.3%)	21 (7.4%)
Corebrovascular events	0	2 (1.0%)	0	6 (1.3%)	9 (3.3%)	20 (2.3%)	3 (3.4%)	27 (9.5%)
Infections and Infestations	28 (39.4%)	63 (31.2%)	70 (42.9%)	182 (38.1%)	134 (48.9%)	360 (41.8%)	40 (46.0%)	123 (43.5%)
APTC events	1 (1.4%)	2 (1.0%)	2 (1.2%)	11 (2.3%)	11 (4.0%)	24 (2.8%)	5 (5.7%)	23 (8.1%)

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



1

TREATMENT-NAÏVE CASES OF NEOVASCULAR AMD

2

RESISTANT CASES OF NEOVASCULAR AMD



AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

VISUAL AND ANATOMICAL OUTCOMES

RESEARCH LETTERS

Dramatic Resolution of Choroidal Neovascular Abnormalities After Single Aflibercept Injection Following Years of Ranibizumab Use

F Rapid response of retinal pigment epithelial detachments to intravitreal aflibercept in neovascular age-related macular degeneration refractory to bevacizumab and ranibizumab

KH Patel¹, CC Chow¹, R Rathod¹, WF Mieler¹, JI Lim¹, LJ Ulanski II¹, YI Leiderman¹, V Arun² and FY Chau¹

NEOVASCULAR AGE-RELATED MACULAR

Aflibercept Therapy for Exudative Age-related Macular Degeneration Resistant to Bevacizumab and Ranibizumab

Conversion to Aflibercept For Chronic Refractory Or Recurrent Neovascular Age-Related Macular Degeneration

BENJAMIN BAKALL, JAMES C. FOLK, H. CULVER BOLDT, ELLIOTT H. SOHN, EDWIN M. STONE, STEPHEN R. RUSSELL, AND VINIT B. MAHAJAN

SIC YOSHIHIRO YONEKAWA, CHRISTOPHER ANDREOLI, JOHN B. MILLER, JOHN I. LOEWENSTEIN, LUCIA SOBRIN, DEAN ELIOTT, DEMETRIOS G. VAVVAS, JOAN W. MILLER, AND IVANA K. KIM

ADRIAN HEN-CHUN FUNG, MBBS, MRCOED, JASON SLAKTER, MD, *†‡ JOHN SURENSEN, MD, *†‡
K. BAILEY FREUND, MD*‡§

Short-Term Outcomes of Aflibercept for Neovascular Age-Related Macular Degeneration in Eyes Previously Treated With Other Vascular Endothelial Growth Factor Inhibitors

Intravitreal Aflibercept for Treatment-Resistant Neovascular Age-related Macular Degeneration

VINCENT Y. HO, STEVEN YEH, TIMOTHY W. OLSEN, CHRIS S. BERGSTROM, JIONG YAN, BLAINE E. CRIBBS, AND G. BAKER HUBBARD, III

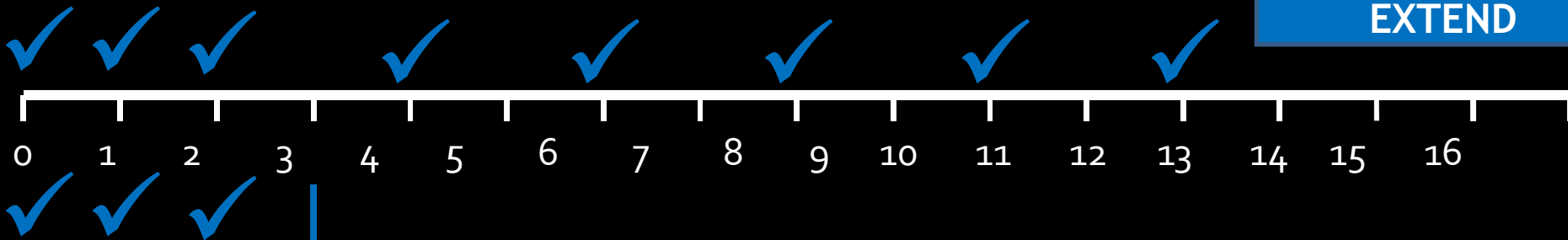
Andrew A. Chang, FRANZCO, PhD,^{1,2} Haitao Li, MBBS, PhD,¹ Geoffrey K. Broadhead, MBBS,^{1,2} Thomas Hong, MScMed, BAppSc,¹ Timothy E. Schlub, BSc(Hons), PhD,³ Wijeyanthy Wijeyakumar, MOTH, BSc,^{1,2} Meidong Zhu, MBBS, PhD²



AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

FLUID RESOLUTION
[~80%]

**TREAT and
EXTEND**



PERSISTENT FLUID
[~20%]

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



A

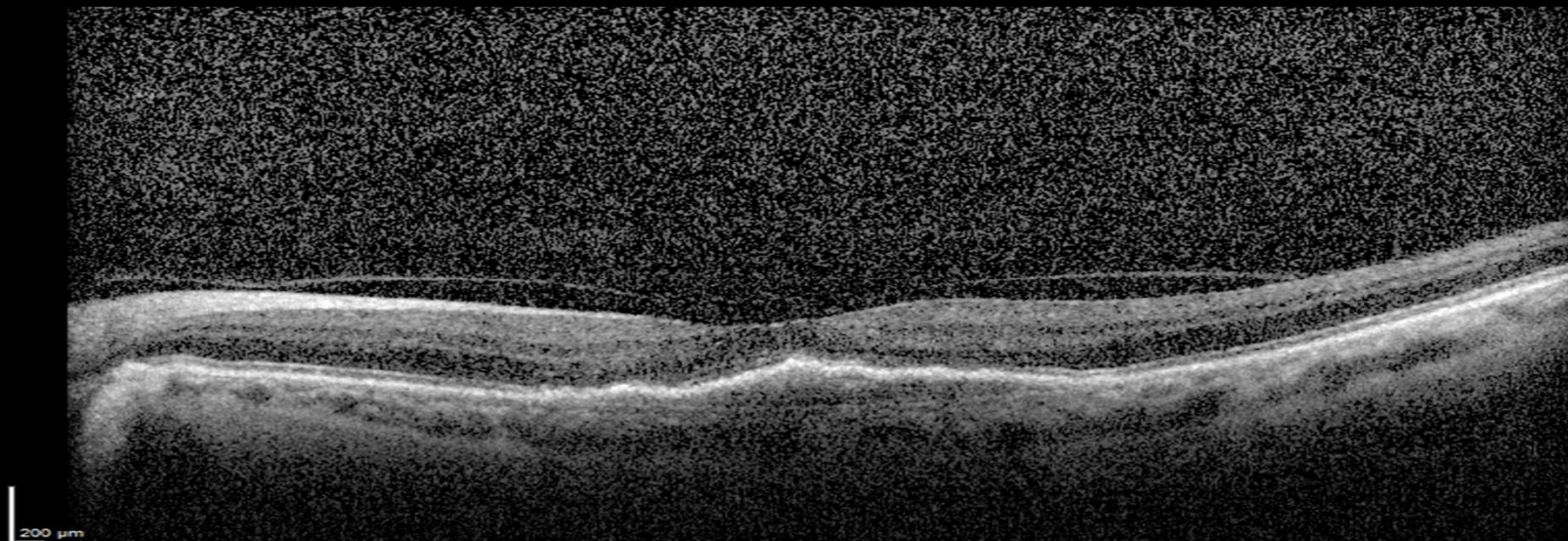
VERIFY LACK OF ANATOMIC RESPONSE TO THERAPY

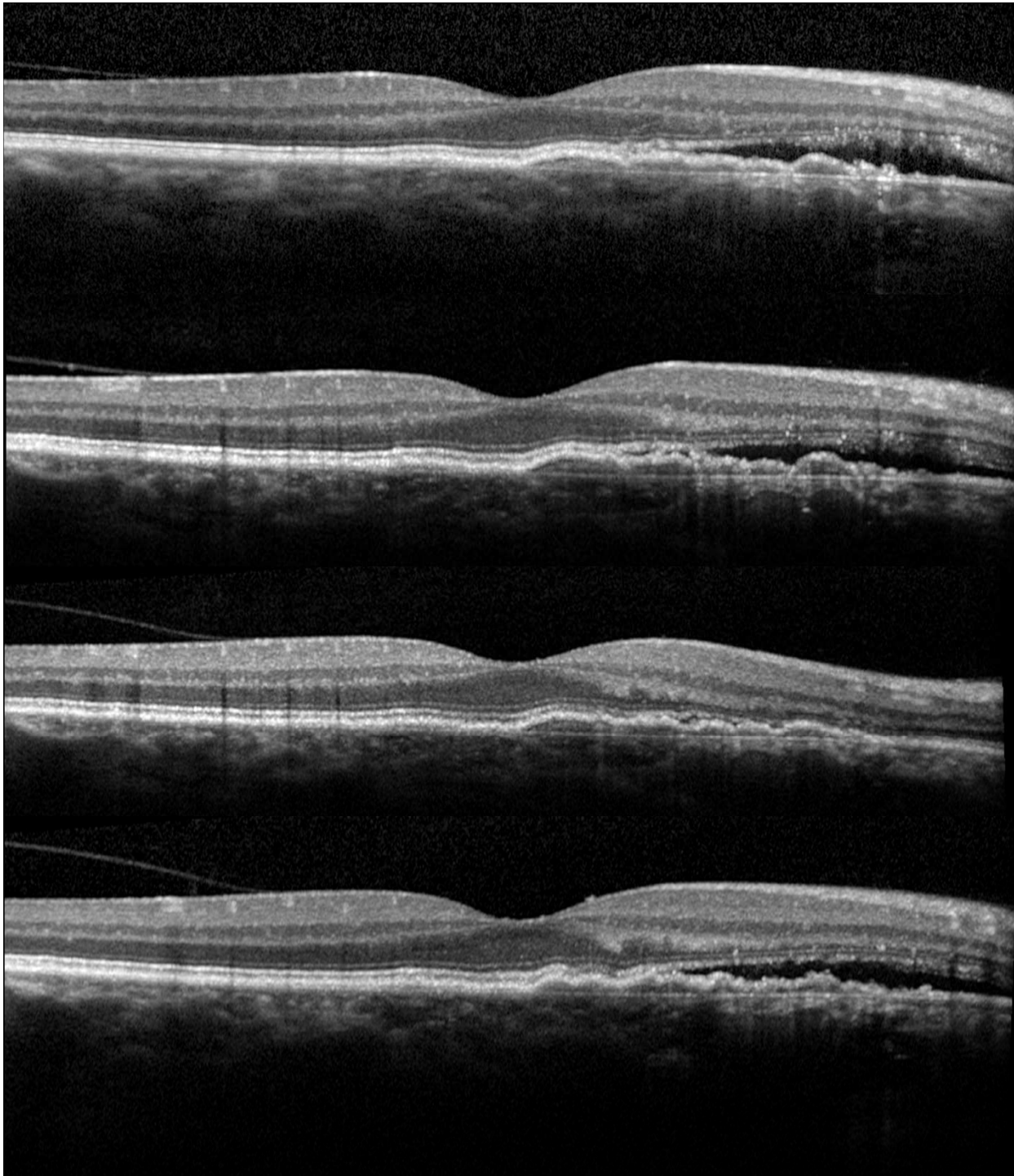
B

PERFORM THE SWAP AFTER INJECTION **#6**

C

INITIATE NEW TREATMENT WITH **3 MONTHLY INJECTIONS**





BASELINE

20/25

LUCENTIS

4 WEEKS

20/30

EYLEA

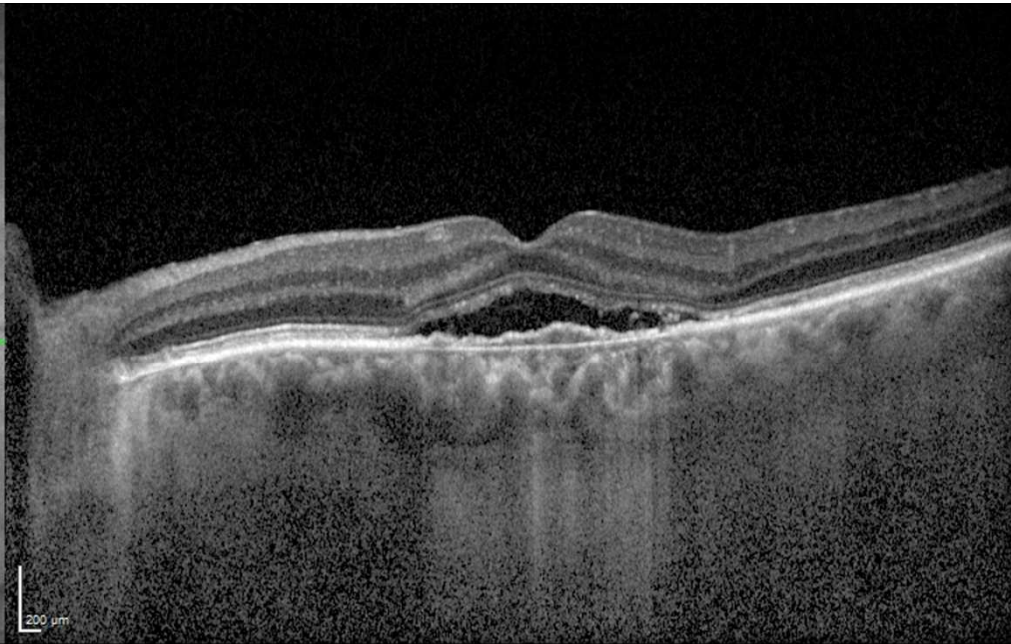
8 WEEKS

20/25

LUCENTIS

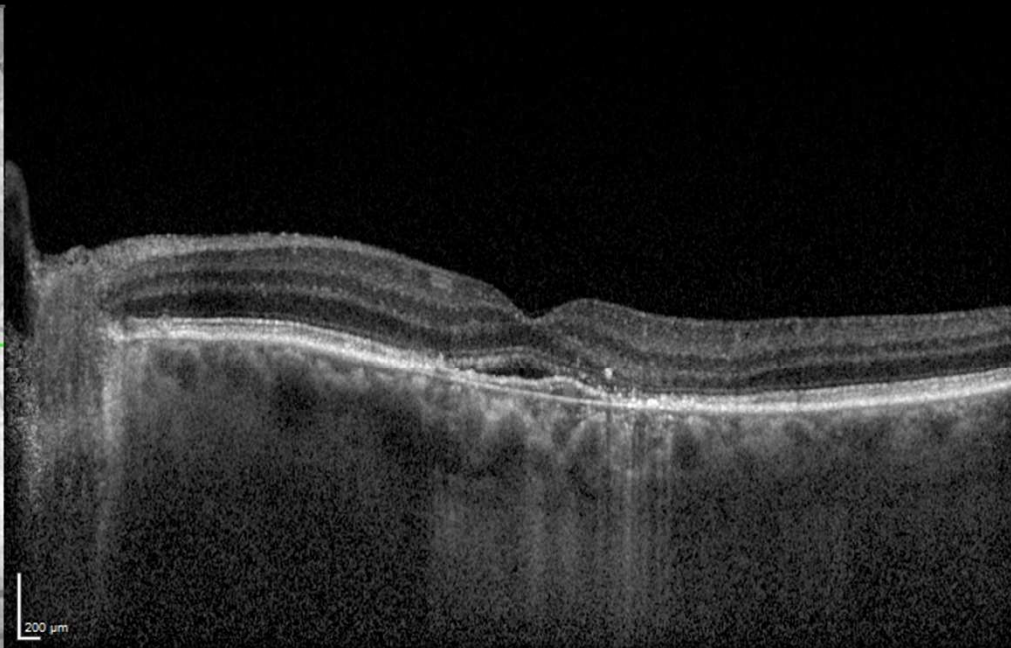
12 WEEKS

20/30



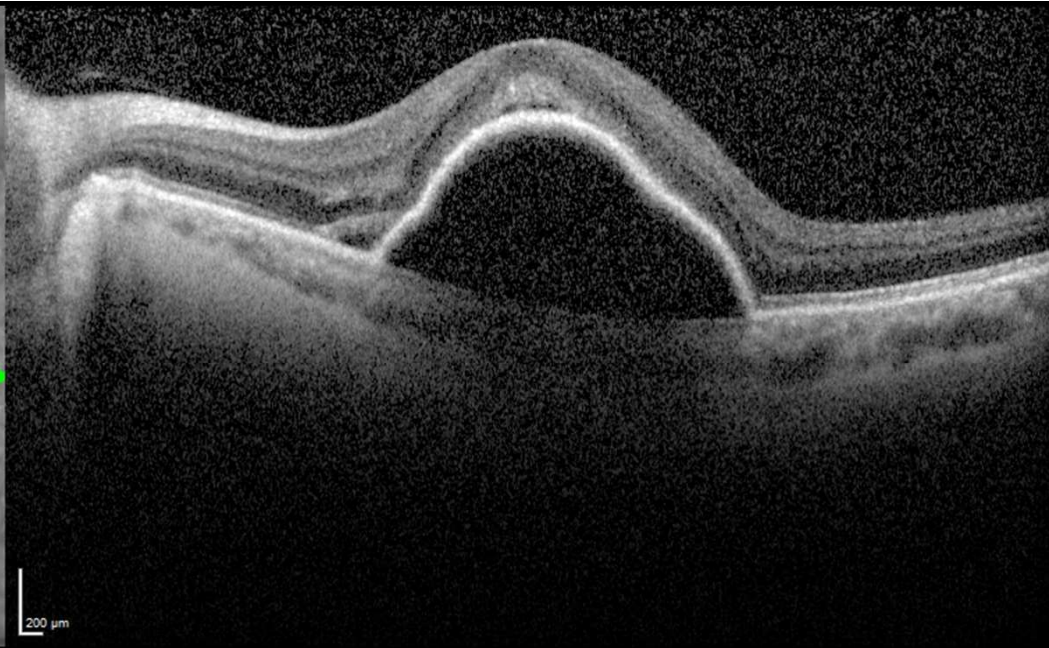
20/60
LUCENTIS 2

17/02/2014, OS



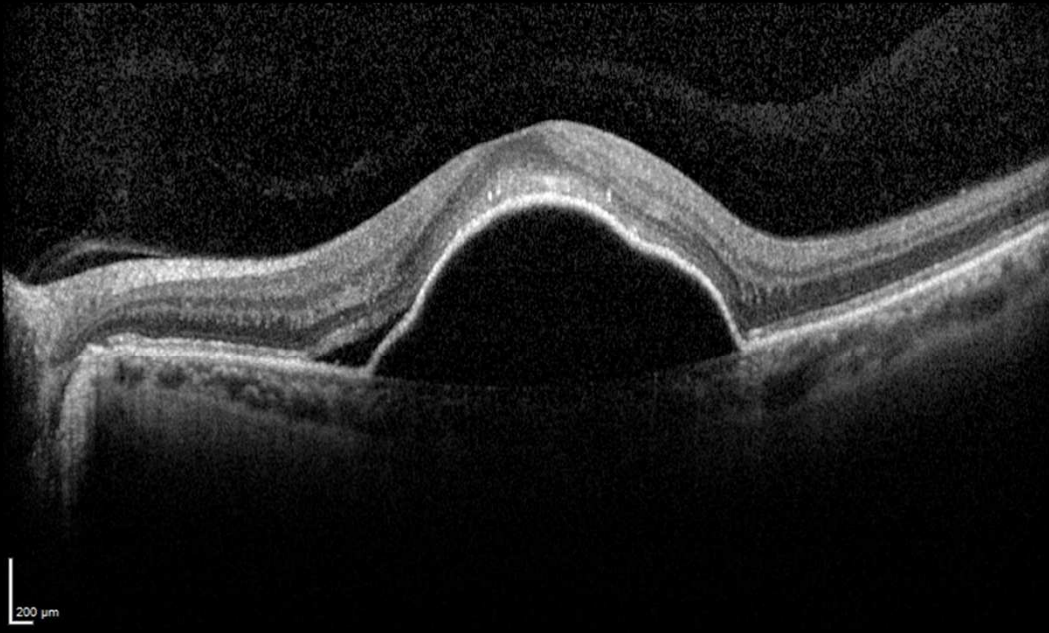
20/50
LUCENTIS 1

05/03/2014, OS



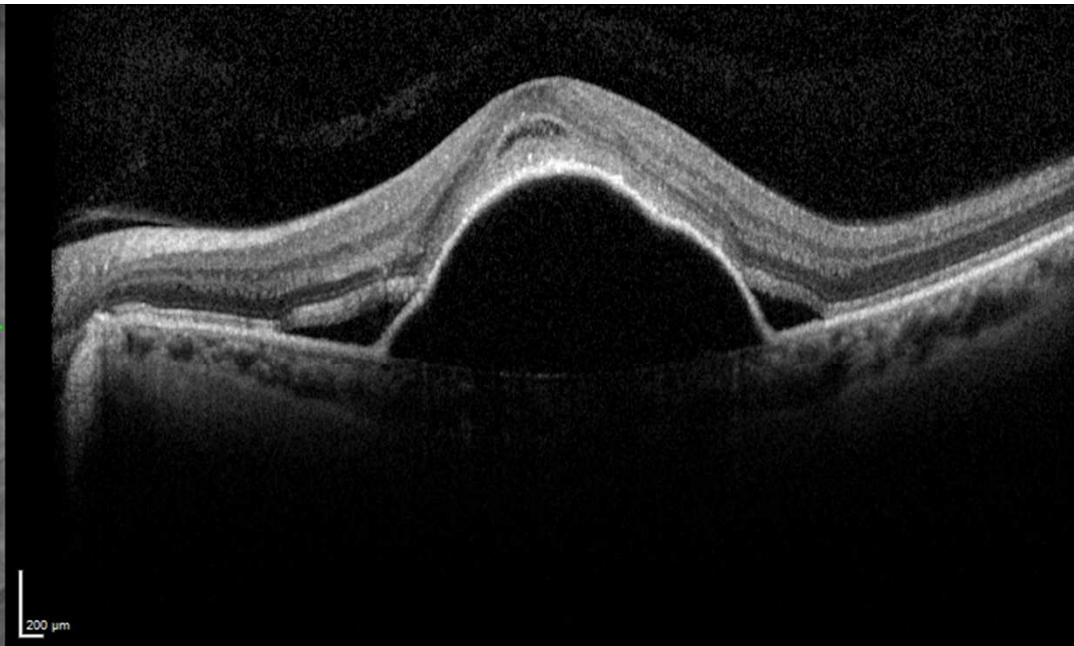
05/08/2013, OS

20/40
LUCENTIS 2



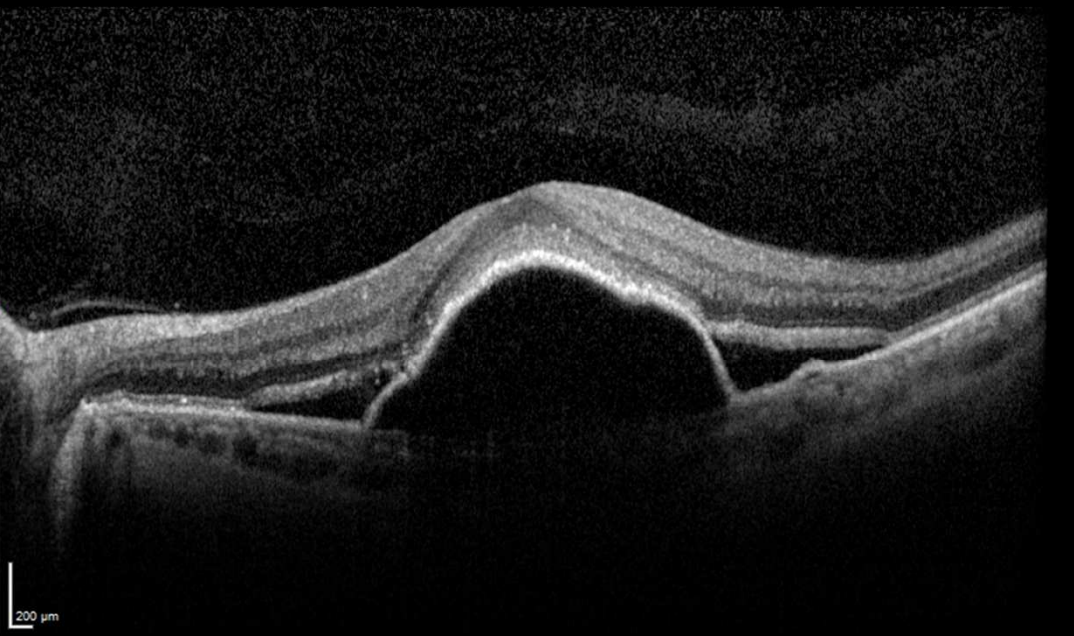
11/09/2013, OS

20/40
LUCENTIS 3



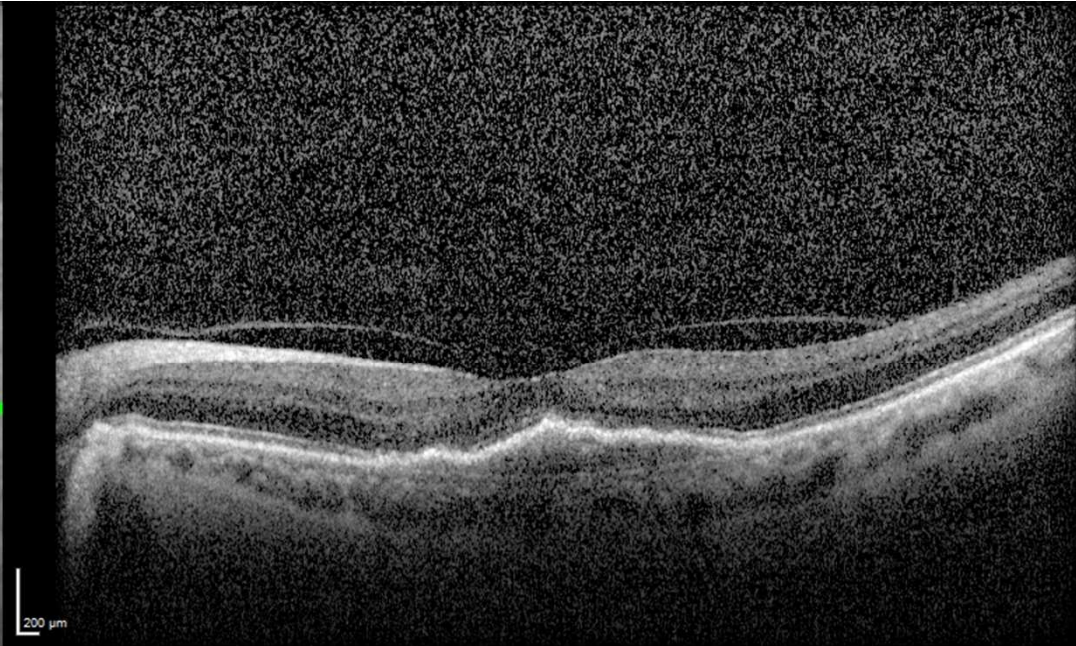
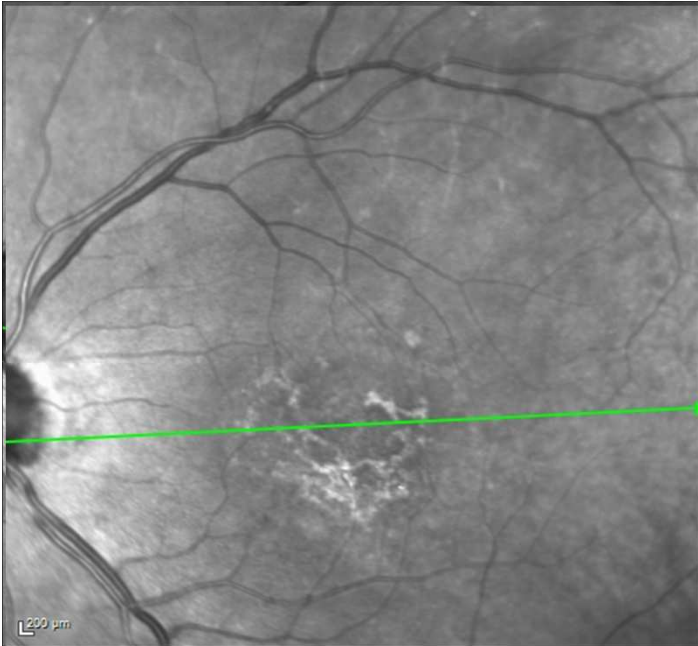
23/10/2013, OS

20/40
LUCENTIS 4



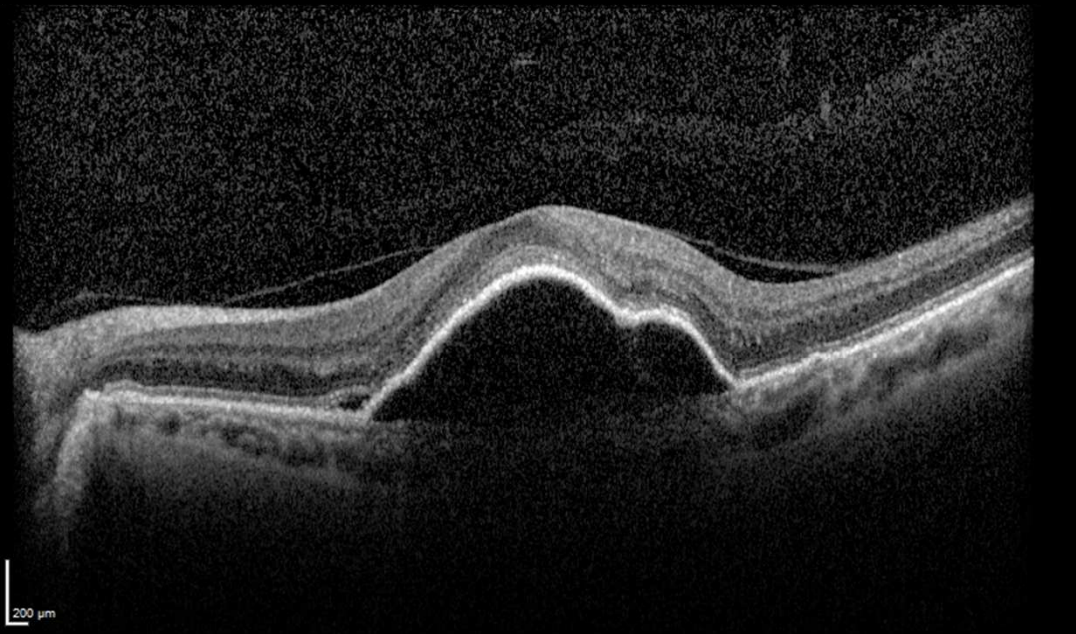
04/12/2013, OS

20/50
LUCENTIS 3



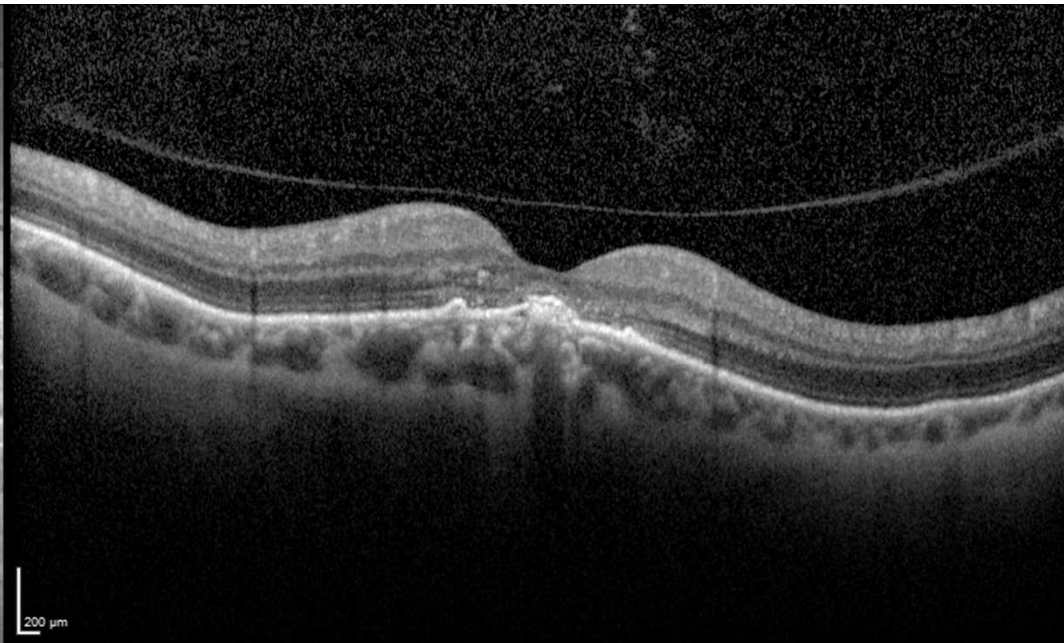
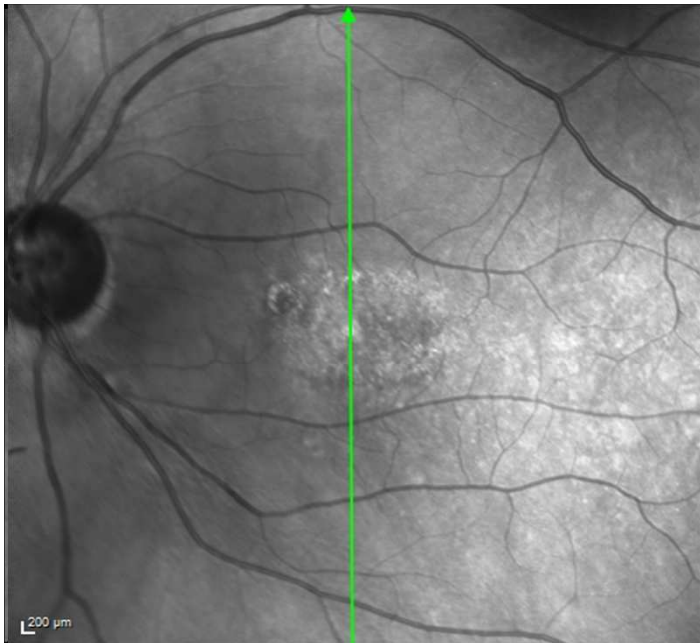
20/30
EYENTIA 6

12/03/2014, OS



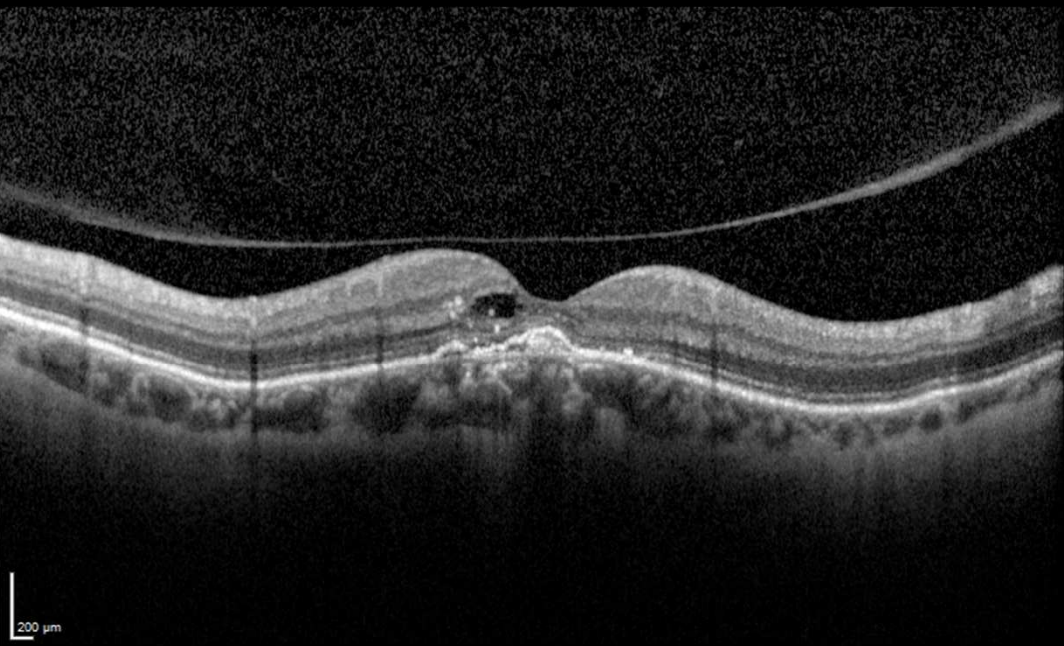
20/50
LUCENTIS 3

12/02/2014, OS



04/03/2014, OS

20/40
EYLEA 3



23/01/2014, OS

20/50
LEVENIA 1

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



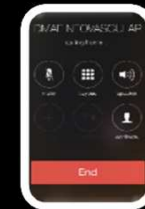
- Classify CNV by FA + SD-OCT
- Strongly consider **EYLEA** as first line therapy for certain cases
 - Loading dose with 3 monthly treatments
 - If persistent fluid ... consider monthly treatment
 - Second and following years ... go for treat and extend

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW



- Strongly consider **EYLEA** as rescue therapy no later than injection #6

- Avoid calling a wrong number



- Loading dose with 3 monthly treatments

- If persistent fluid ... keep treating monthly

- Second and following years ... probably go for treat and extend

AMD MANAGEMENT ...

What changes with a new player

AMD CLASSIFICATION AND RATIONALE FOR THERAPEUTIC STRATEGIES

IDENTIFICATION AND MANAGEMENT OF RESISTANT NEOVASCULAR AMD

AFLIBERCEPT FOR NEOVASCULAR AMD: WHY, WHEN, AND HOW

AMD MANAGEMENT ...

What changes with a new player



Roberto Gallego-Pinazo

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University and Polytechnic Hospital La Fe, Valencia, Spain