Ankara ÜTF- Ocak 2016

YBMD DE Anti-VEGF CEVAPLARI

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Anti-VEGF cevapları

Erken Dönem…Geç Dönem

AYLIK DÜZENLİ ENJEKSİYONLAR YAPILMIŞ HASTALARDA!

Anti-VEGF cevapları

Erken Dönem

- ÇOK İYİ CEVAP (İLK 3 DOZ İLE SIVI YOK, GK↑)
- SUBOPTİMAL CEVAP (GK=↑ SIVI↓ TAM DEĞİL)
- STABİLİZASYON
  - İLK 3 DOZ İLE SIVI AYNI GK: AYNI
- CEVAPSIZLIK (İLK 3 DOZ İLE SIVI↑ VEYA GK↓, Hemoraji (+))
- HEMORAJİK CEVAP (İLK DOZLARDA GİDEREK ARTAN HEMORAJİLER)
- KOMPLİKASYONLAR (RPE YIRTIĞI, ATROFİ)

Anti-VEGF cevapları

Erken Dönem

- ÇOK İYİ CEVAP (İLK 3 DOZ İLE SIVI YOK, GK↑)
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- CEVAPSIZLIK (İLK 3 DOZ İLE SIVI↑ VEYA GK↓, Hemoraji (+): Aktivite skoru!)
- HEMORAJİK CEVAP (İLK DOZLARDA GİDEREK ARTAN HEMORAJİLER)
- KOMPLİKASYONLAR (RPE YIRTIĞI, ATROFİ)

Anti-VEGF Cevapları
Uzun Dönem

- ÇOK İYİ CEVAP VERENLER: Yıllarca ilave tedaviye ihtiyaç duymayabilir.
- YAVAŞ CEVAP VERENLER: >3 sıra kazananların %8-13'ü 3 -12. aya kadar olmuş (CATT, HARBOUR)
- SIK TEDAVİ GEREKTİRENLER
    - Aylık tedaviye rağmen persistan sıvısı olanlar
    - Tedaviye iyi cevap verip sık reaktive olanlar
    - RAP, Geniş occult membranlar (RPE-altı)
- BAŞLANGIÇTA İYİ CEVAP (İLK 3 DOZ İLE SIVI YOK)→GİDEREK AZALAN CEVAP: TAŞİFLAKSİ / TOLERANS

ANTİ-VEGF TEDAVİDE İSTENMEYEN SONUÇ

- GÖRMEDE AZALMA!
- HER GÖRMEDE AZALMA CEVAPSIZLIK MIDIR?
- CEVAPSIZLIĞI NASIL TARİF EDELİM?

Yaş Tip YBMD
Doğal Gidiş

- Doğal gidişten daha iyi görsel prognozu olan tüm durumlar tedaviye olumlu cevap göstergesidir.

- Doğal Gidiş: MARINA & PIER

Holz ,F., et al. IOVS, January 2010, Vol. 51, No. 1- 405-412.

Yaş Tip YBMD
Doğal Gidiş

- GK de yılda 12.6 harf kayıp ortalama doğal hastalık progresyonu olarak tanımlanmıştır.

- MARINA ve PIER deki sham tedavi hastalarından: hastalar arası SD: 20 harf/yıl!

- Yavaş (5 harf/yıl), orta (12.6 harf/yıl), ve hızlı (19 harf/yıl) progresyon gösterenler

  Holz ,F., et al. IOVS, January 2010, Vol. 51, No. 1-405-412.

ANTİ-VEGF TEDAVİ CEVAPSIZLIK TANIMI

- GÖRMEDE AZALMA?
- OCT DE SIVIDA ARTIŞ?
- LEZYONDA BÜYÜME?
- YENİ HEMORAJİ?
- SIK TEDAVİ İHTİYACI DUYMA DURUMU?
- CEVAPSIZLIĞI NASIL TARİF EDELİM?

LEZYON AKTİVİTE SKORUNDA ARTIŞ OLMASI

KLİNİK LEZYON AKTİVİTE SKORLAMASI

Hemoraji	Yok Azalmış Aynı (başlangıç) Artmış	0 1 2 3
OCT Subretinal sıvı / retinal kalınlaşma / PED	Yok Azalmış Aynı (başlangıç) Artmış	0 1 2 3
FFA	Boyanma yok/pencere defekti Skar boyanması/PED Geç sızıntı	0 1 2
Lezyon boyutu (FA'da lezyon alanı)	Azalmış Aynı (başlangıç) Artmış	0 1 2
Görme (objektif)	Artmış Aynı (başlangıç) Azalmış	0 1 2
(Subjektif)	Artmış Aynı (başlangıç) Azalmış	0 1 2

ANTİ-VEGF TEDAVİ İSTENMEYEN CEVAPLARI

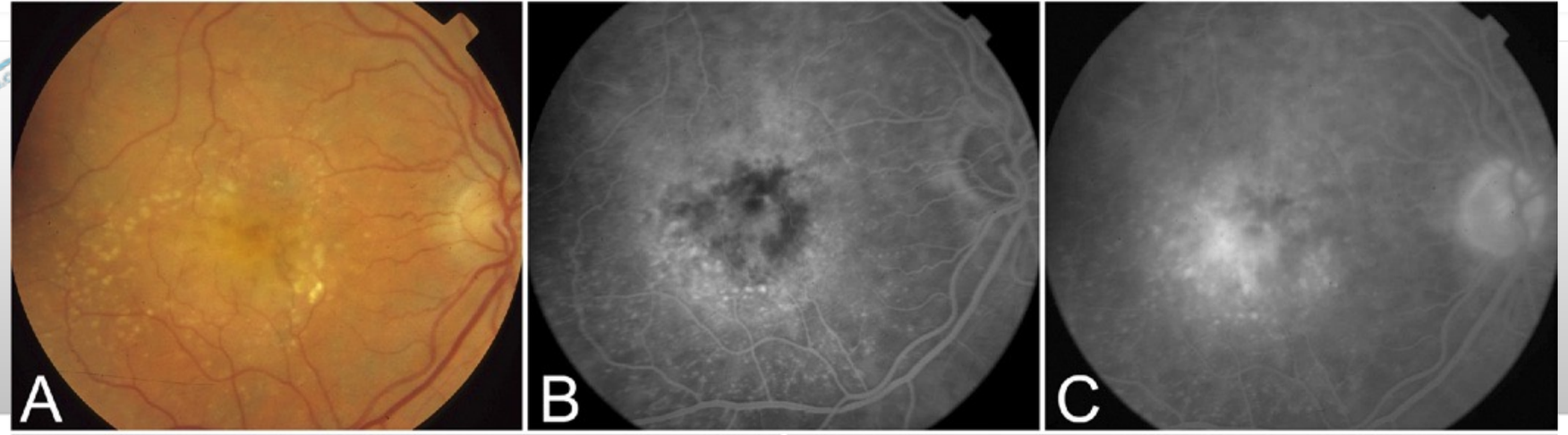
Lezyon aktif değil

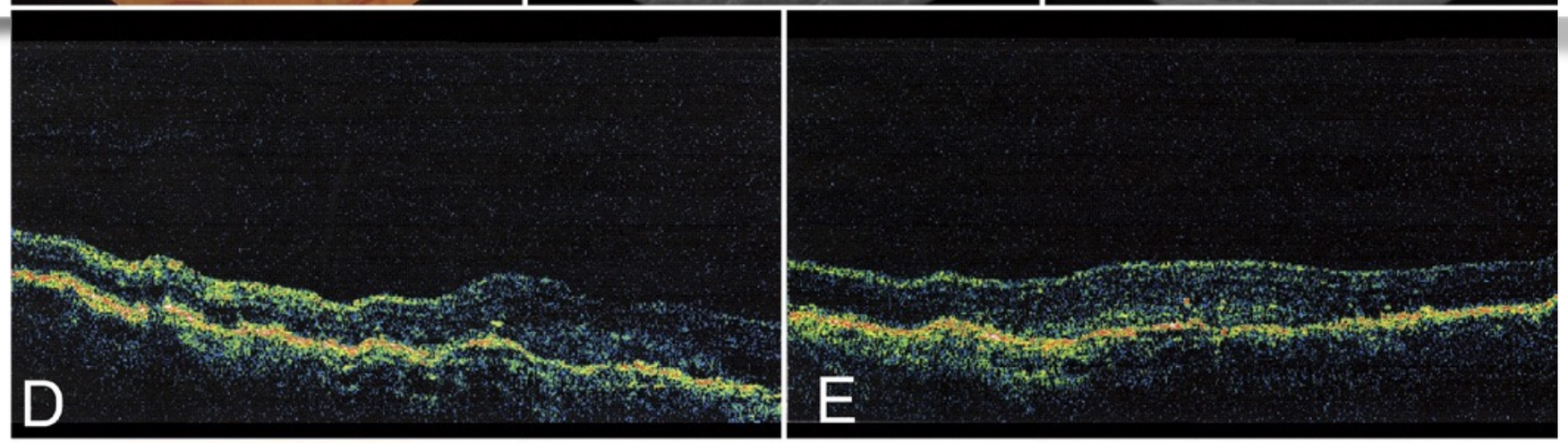
RPE ve fotorec. Atrofisi / Subfoveal fibrozis

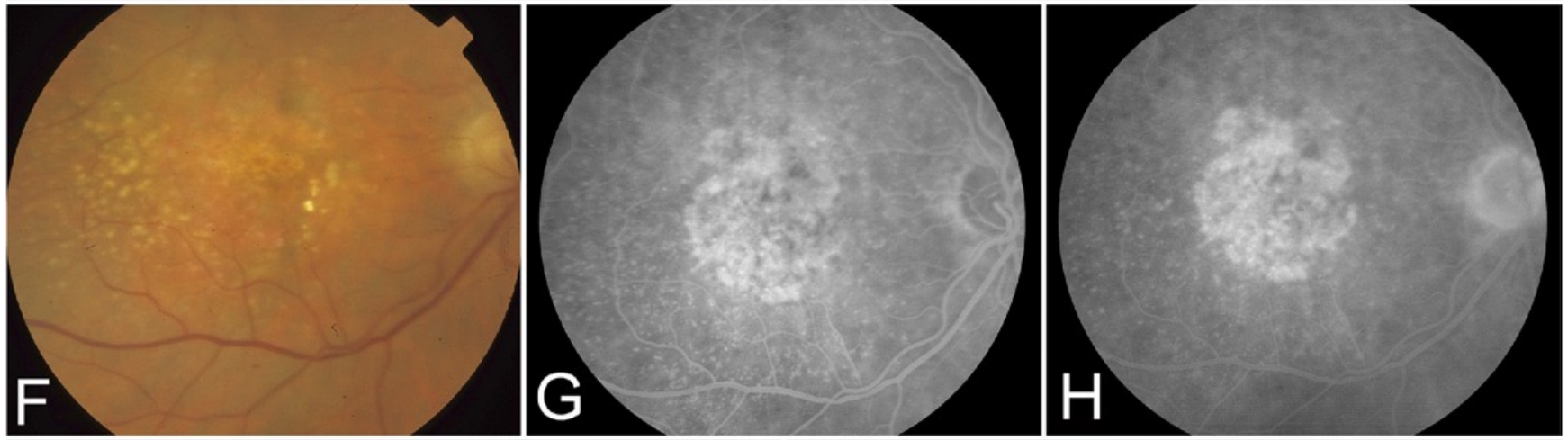
Lezyon aktif

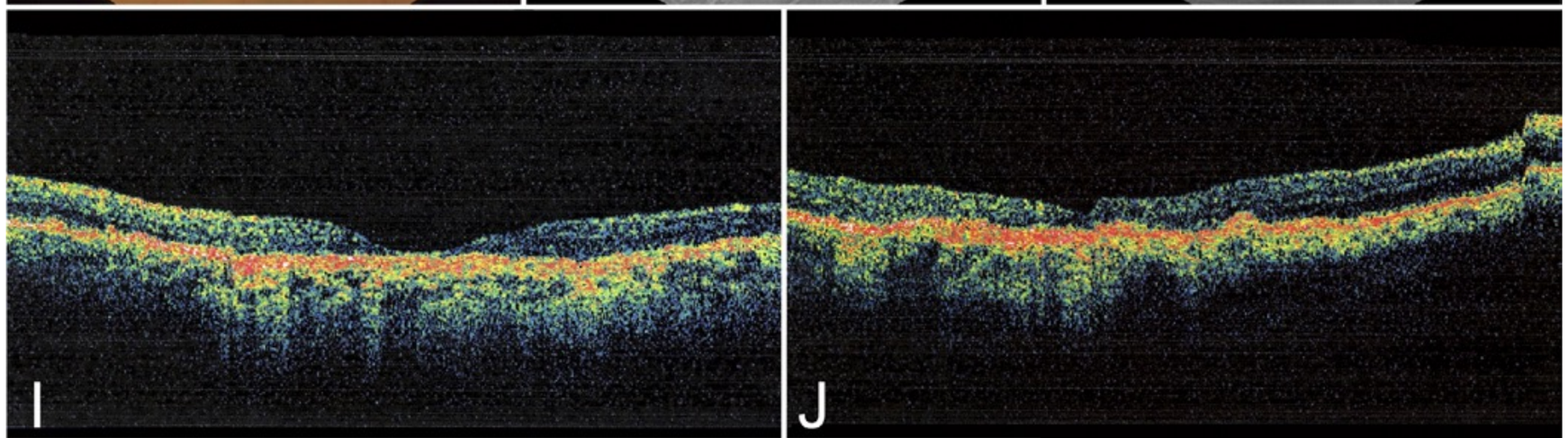
Rekürren, persistan veya ilerleyen exudatif hastalık

(Anti-VEGF tedaviye rağmen)


A
B
C


D
E


F
G
H


I
J

ANTİ-VEGF TEDAVİ CEVAPLARI LEZYON AKTİF DEĞİL GK↓

- RPE ATROFİSİ
  - NV gerilemesi…. Dış retina katmanlarında iskemi?
  - Anti-VEGF: Nöroproteksiyon (-)?
- FIBROZİS NEDENİYLE (ANTİ-PDGF-Fovista!)

ANTİ-VEGF TEDAVİ CEVAPLARI

LEZYON AKTİF GK↓

- Rekürren, persistan veya ilerleyen exudatif hastalık
- LEZYON AKTİVİTESİ YÜKSEK!

ANTİ-VEGF TEDAVİDE İSTENMEYEN CEVAP

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ANTİ-VEGF TEDAVİDE İSTENMEYEN CEVAP

- SUBOPTİMAL CEVAP (↓↓ TAM DEĞİL)
- STABİLİZASYON/PARSİYEL CEVAP (İLK 3 DOZ İLE SIVI VE GK: AY

YAVAŞ CEVAP VEREN GRUP???

Anti-VEGF Tedavide Yavaş Cevap Verenler

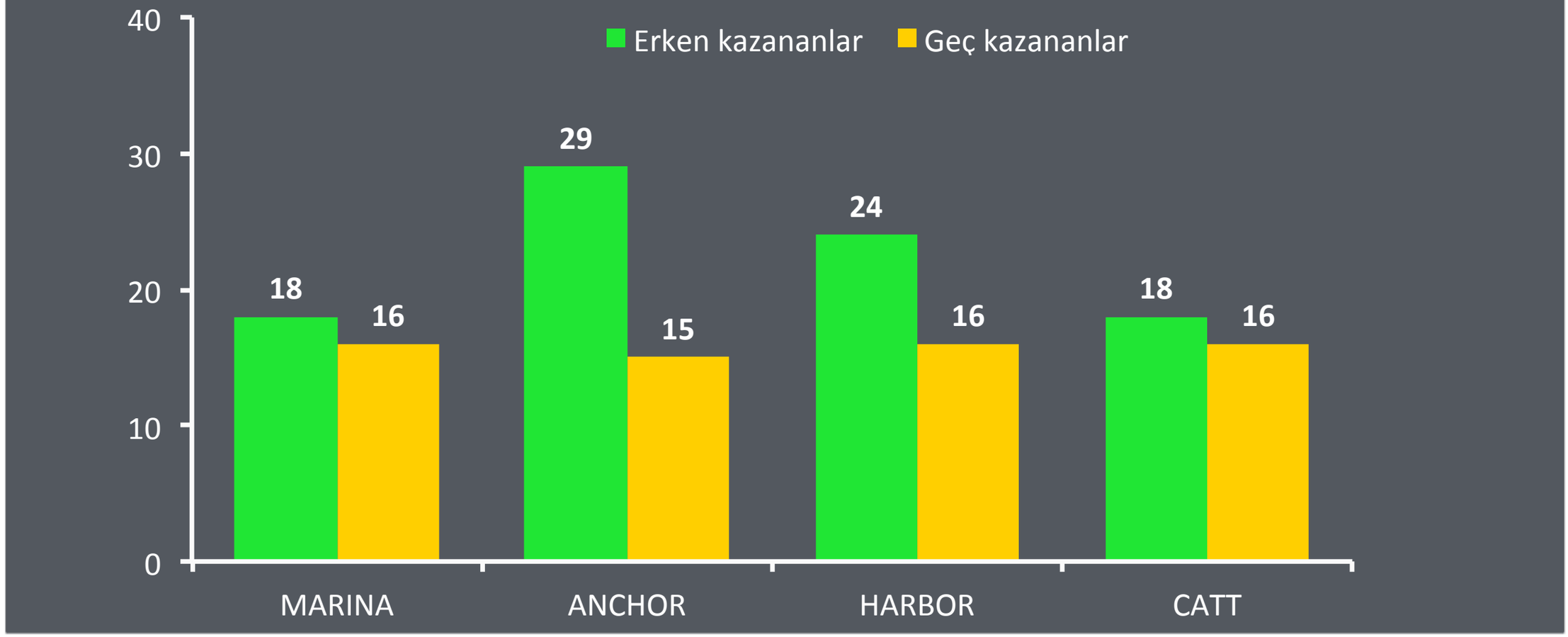
- nYBMD'de ranibizumab tedavisi ile erken ve geç ≥15 harf kazananlar: ANCHOR, MARINA, HARBOR ve CATT çalışmalarından retrospektif bir analiz

- Richard Gale, Jean Francois Korobelnik, Yit Yang, Tien Y. Wong.

- Dreyer R, et al. ARVO, 2013 (poster)

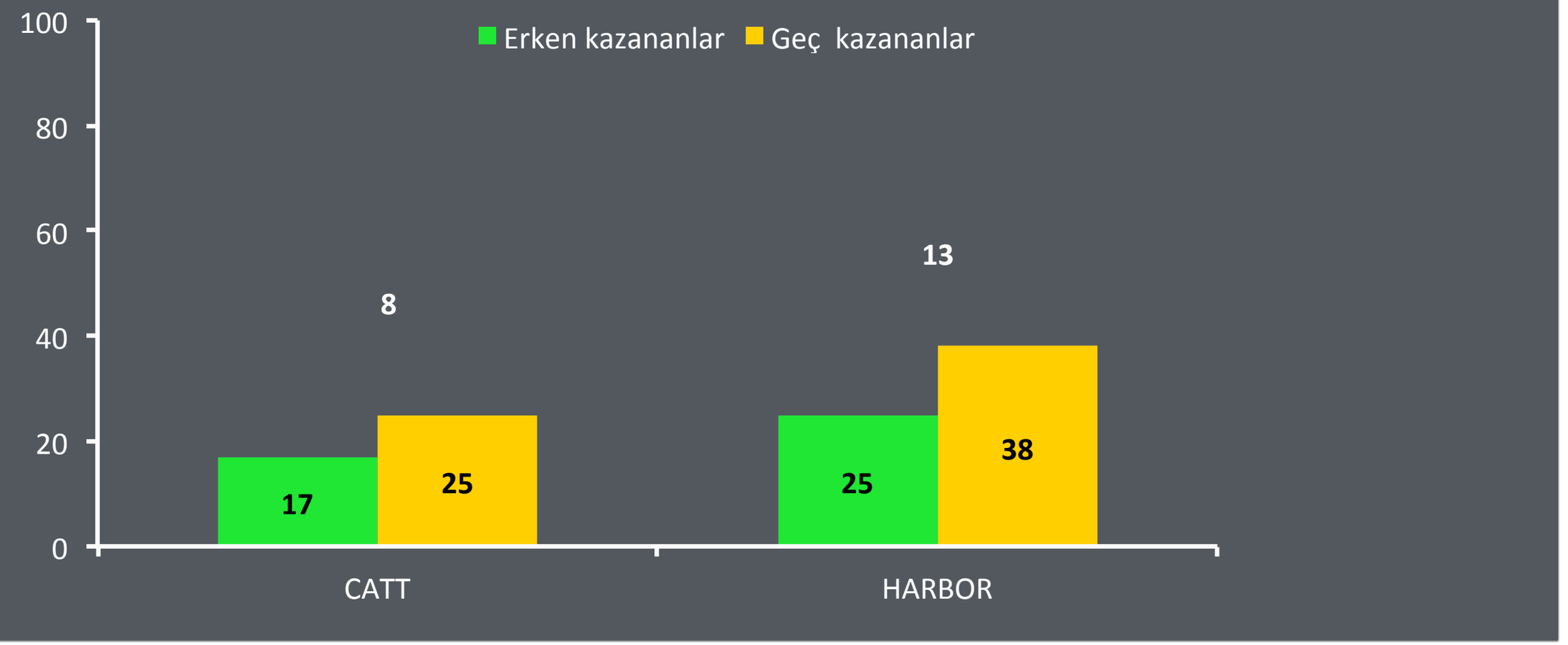
Anti-VEGF Tedavide Yavaş Cevap Verenler

nYBMD çalışmalarında aylık ranibizumab doz uygulaması ile erken ve geç ≥15 harf kazanımı olan hastaların oranı



Anti-VEGF Tedavide Yavaş Cevap Verenler

Ranibizumab PRN doz uygulama rejimi ile erken ve geç ≥15 harf kazanımı olan hasta oranı



ANTİ-VEGF TEDAVİDE İSTENMEYEN CEVAP

- SUBOPTİMAL CEVAP (GK=↑ SIVI↓ TAM DEĞİL)
- STABİLİZASYON CEVABI (İLK 3 DOZ İLE SIVI VE GK: AYNI)
- CEVAPSIZLIK (İLK 3 D[illegible] VE GK↓ HEM.)
- HEMORAJİK CEV[illegible]K DOZLARDA GİDEREK ARTAN HEMORAJİLER)
- TAŞİFLAKSİ-TOLERANS
- KOMPLİKASYONLAR (RPE YIRTIĞI, ATROFİ)

DİRENÇ???

ANTİ-VEGF TEDAVİDE DİRENÇ

- YANLIŞ TANI (%46.2)

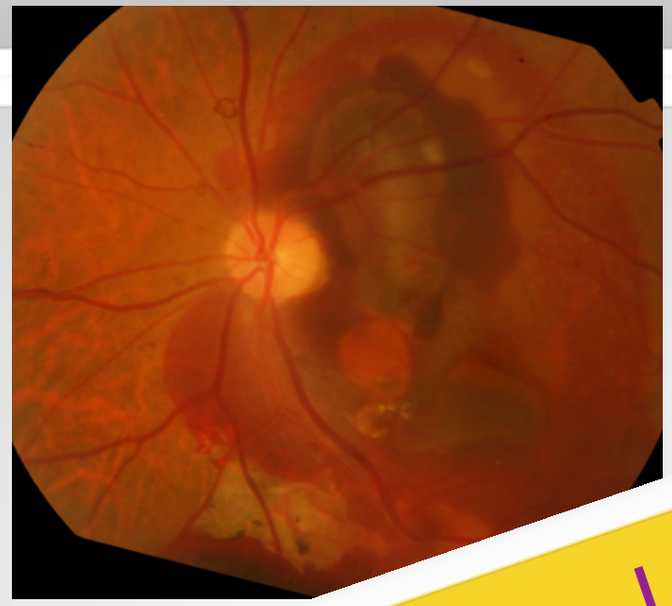
  -PCV, RAP, VİTELLİFORM, SSKR

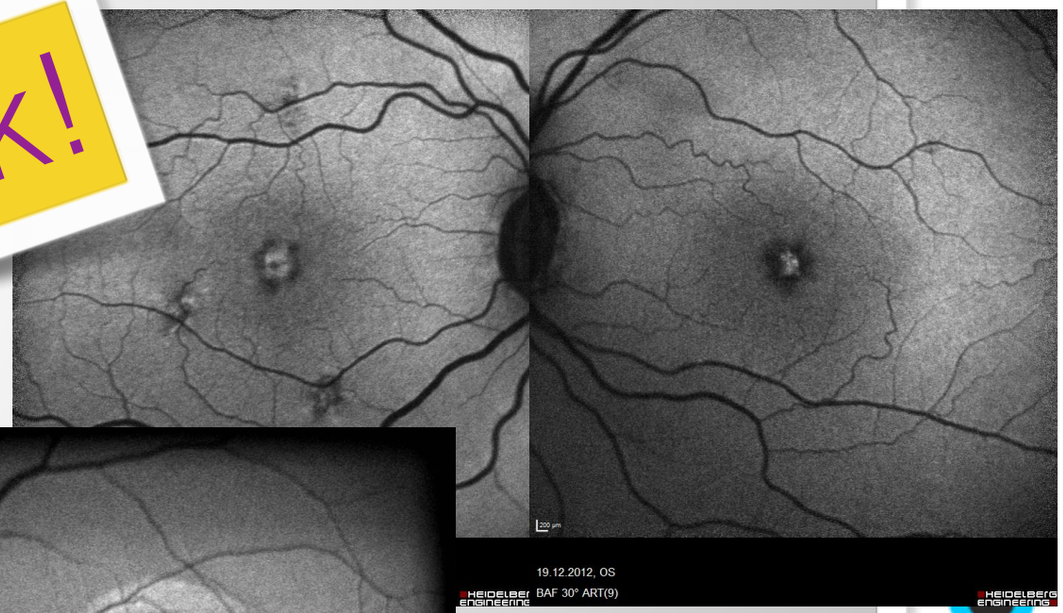
- TAŞİFLAKSİ-TOLERANS (%22)
- CEVAPSIZLAR (%26.9)
- HEMORAJİK CEVAP
- KOMPLİKASYONLAR: RPE yırtığı, atrofi, skar oluşumuna bağlı görme kaybı (%11.6)

Manoj SM. Why does anti-VEGF treatment fail in AMD. Kerala Journal of Ophthalmology. 2011.

YANLIŞ TANI

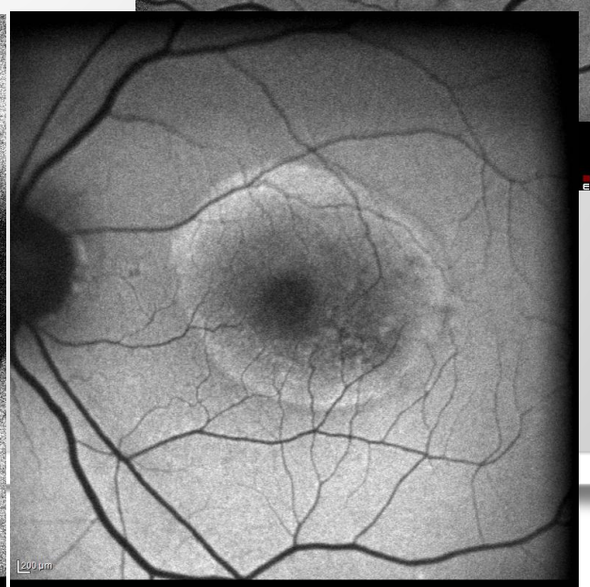
- **PCV**
- **RAP**
- **VİTELLİFORM LEZYONLAR**
- **SSKR**





Drusen yok!

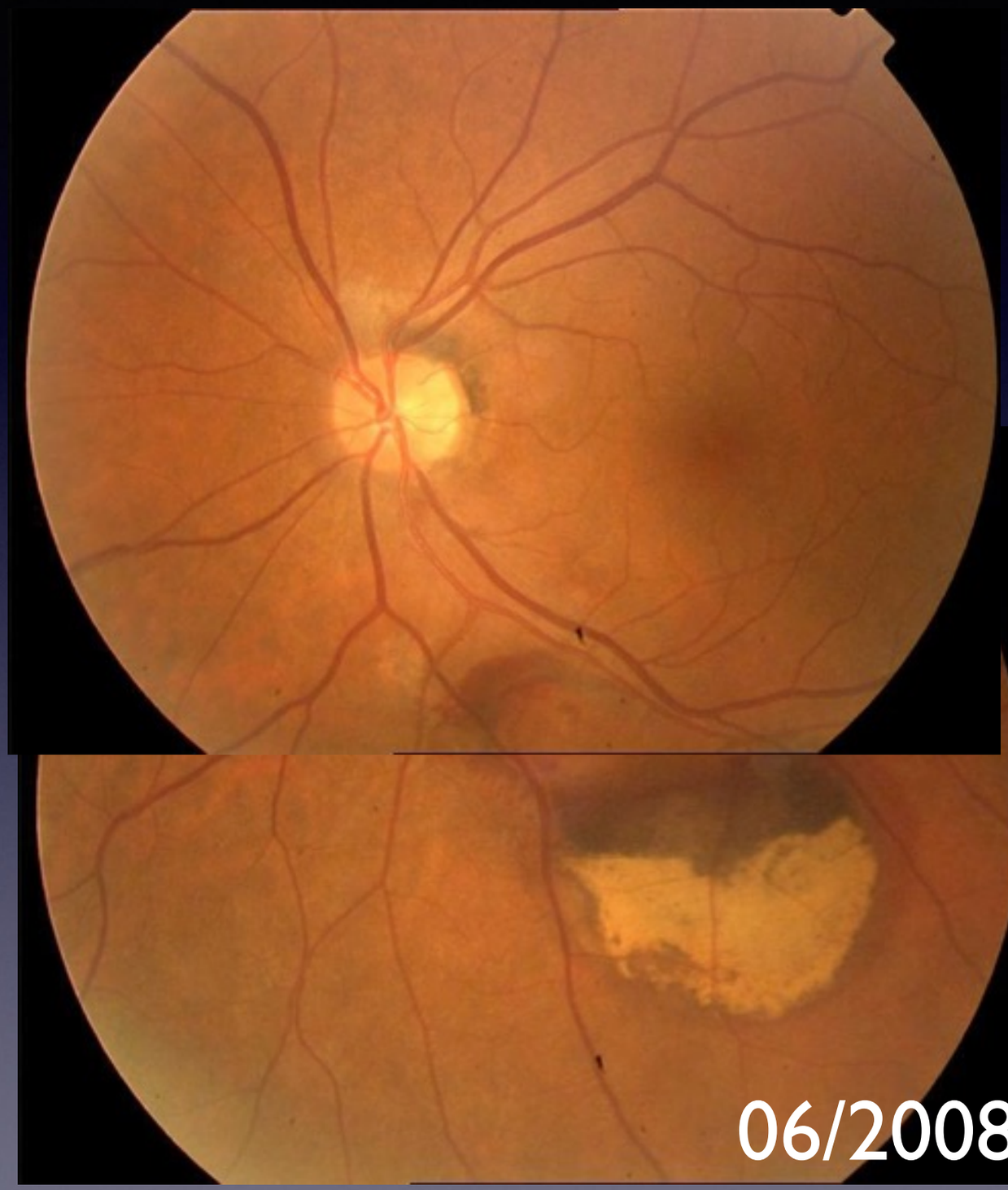




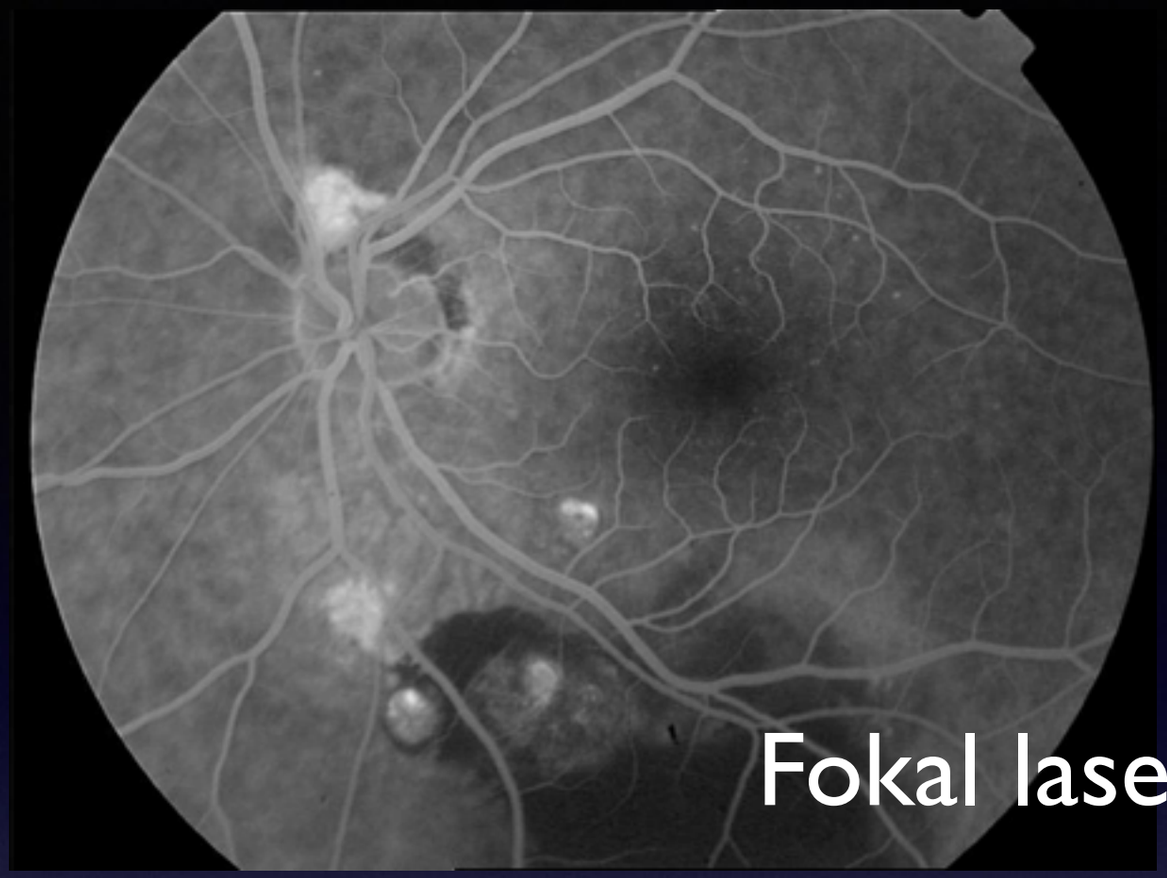
PCV

- YBMD nin alt tipi
- Tüm yaş tip YBMD %8–13 (beyaz ırk), %24–50 (asyalı)
- Drusen yok, Yavaş seyir!
- Peripapiller yerleşim gösteren turuncu renkli subretinal polipler, dallanan dilate damarlar
- Sıklıkla RPE altı kanamalar
- TANI: ICG şart
- TEDAVİ: PDT+Anti-VEGF

64y old M, VA: 20/20



06/2008

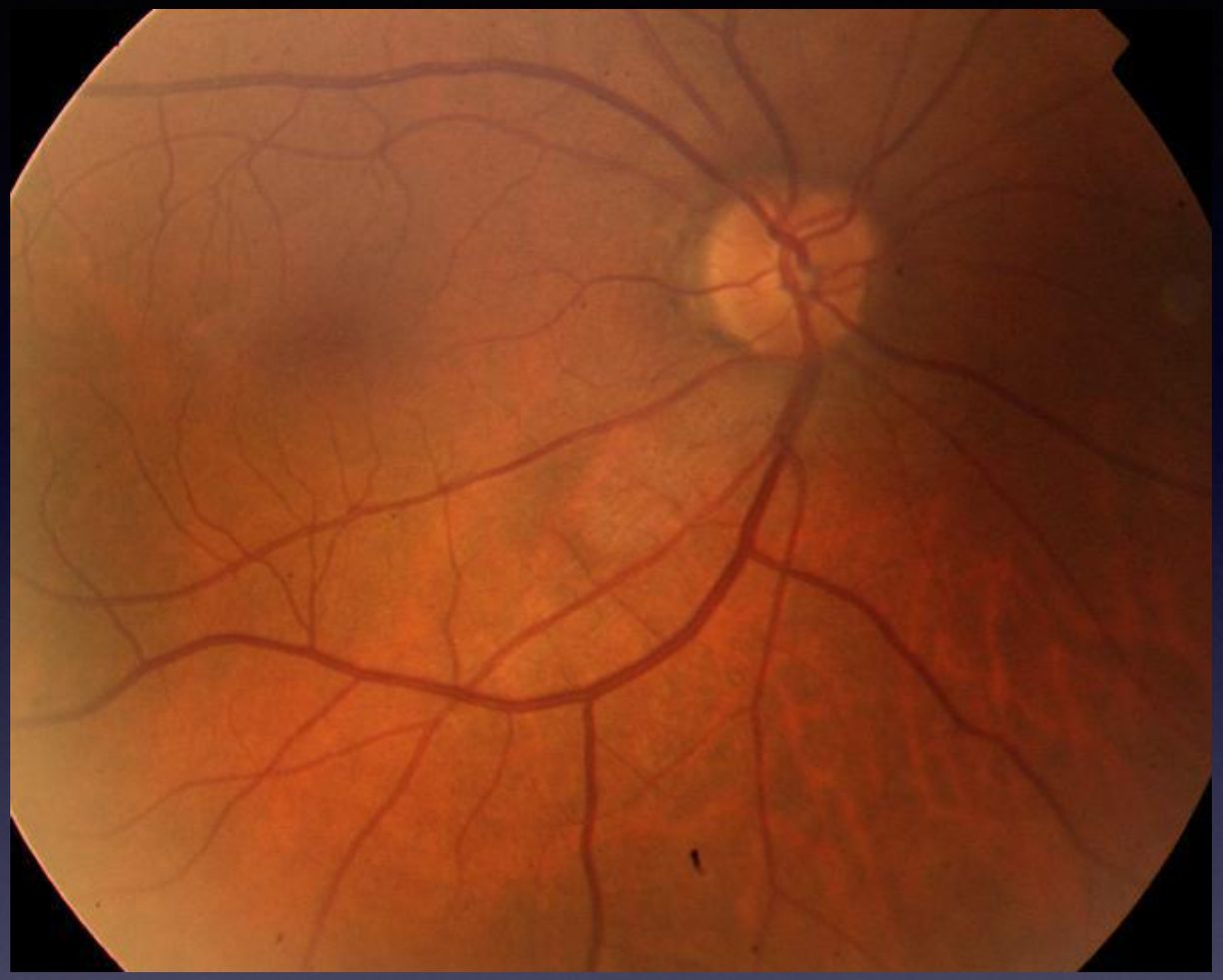


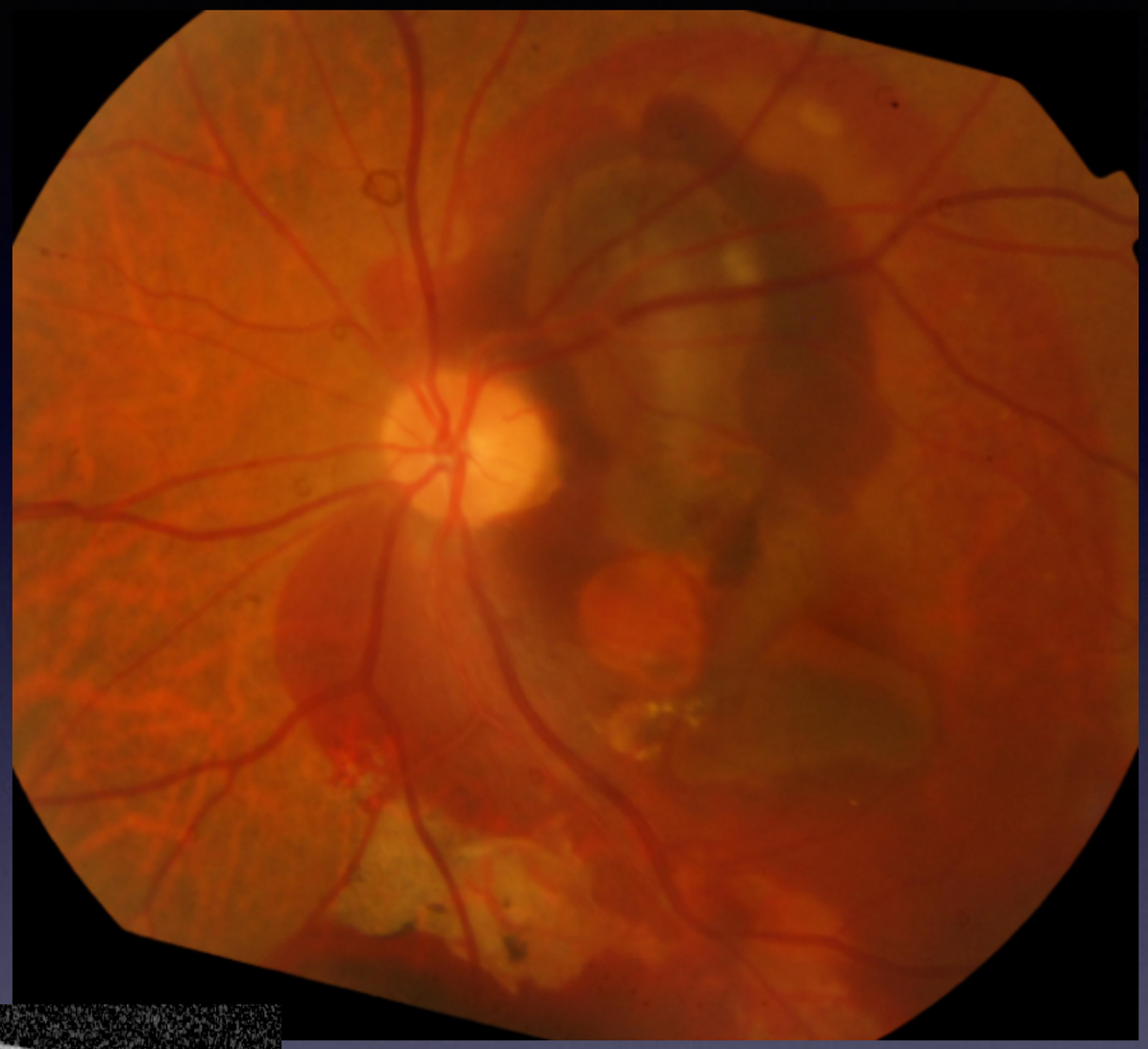
Fokal laser

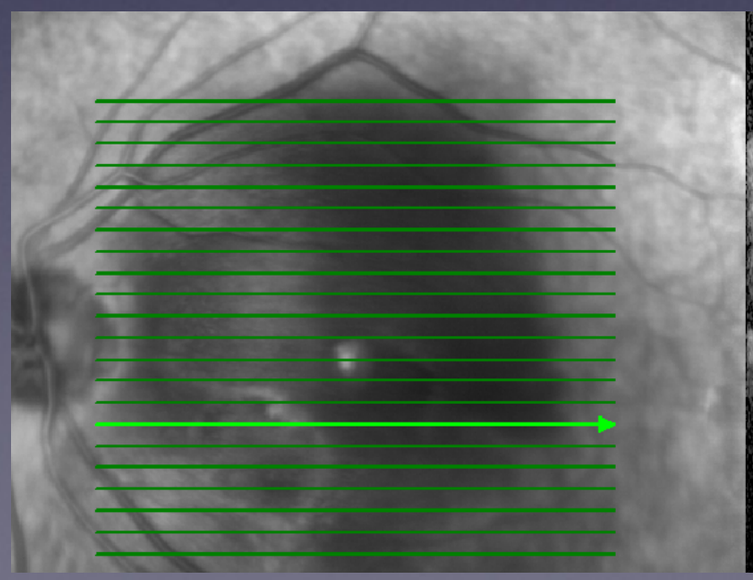


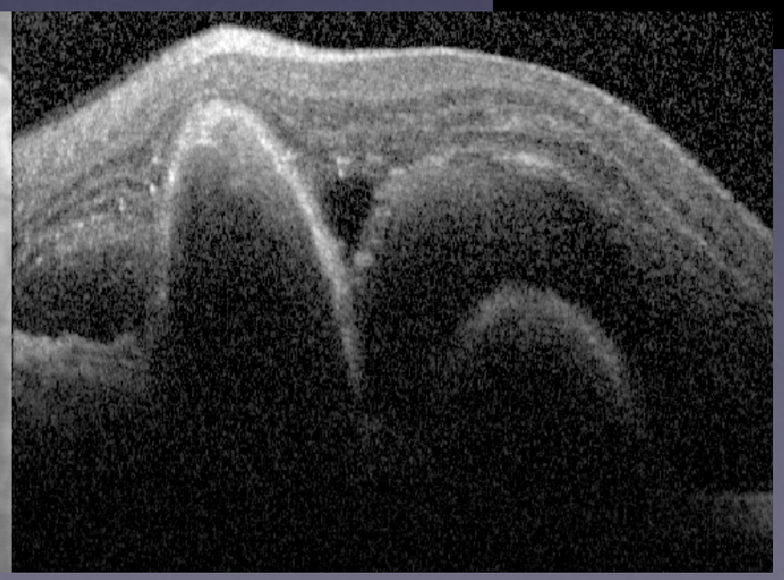
12/2009

09/2012, VA: CF 2m (L)



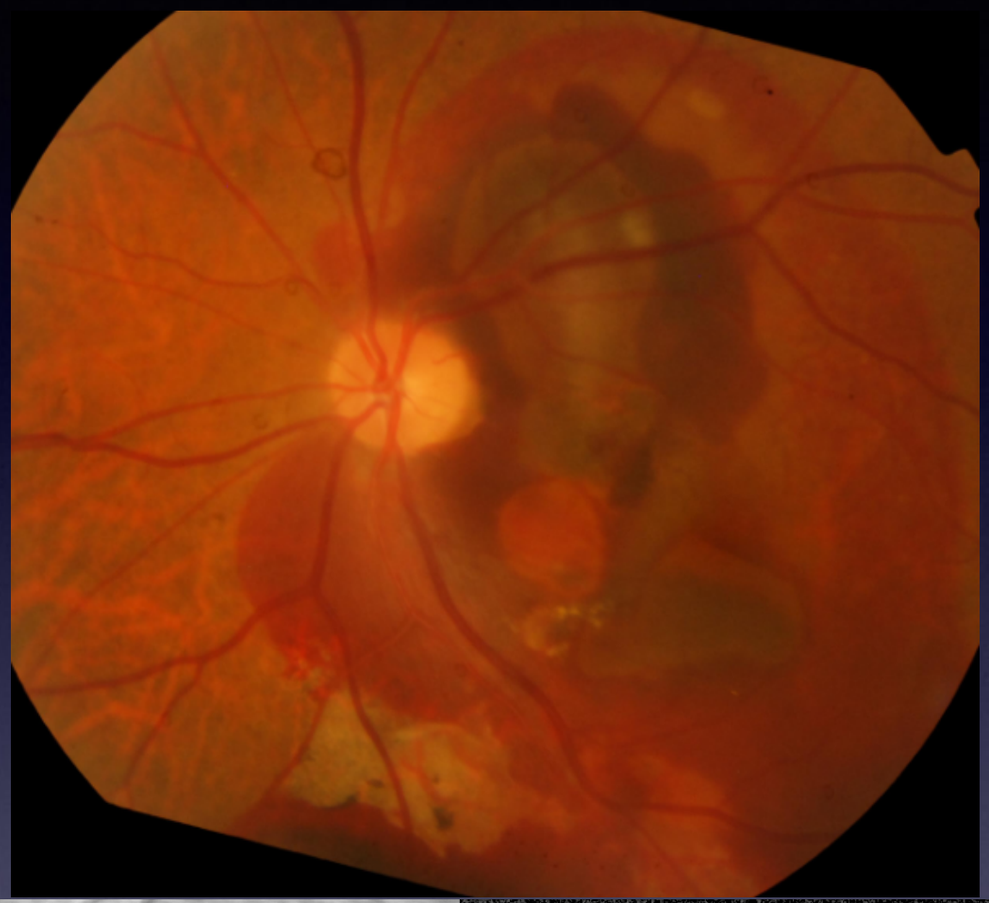


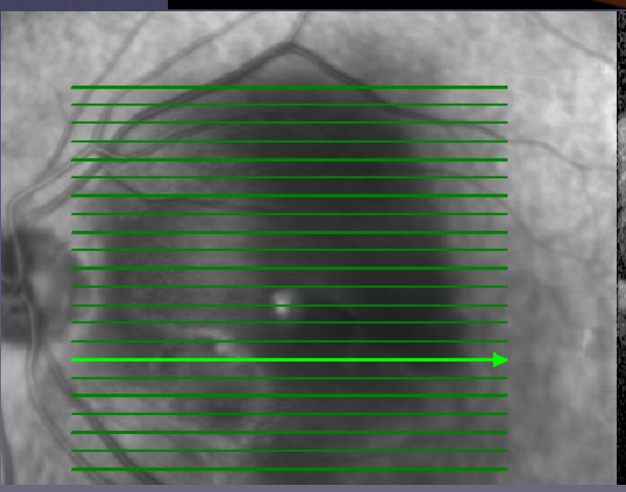


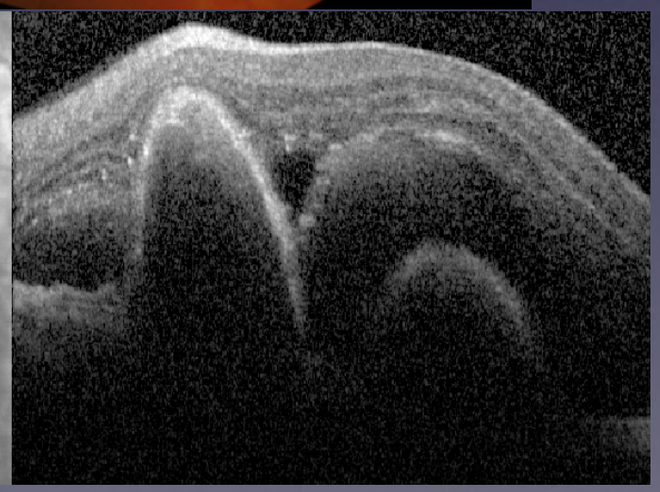


- SF6 Gas + IV tPA (50µg/0.05ml) +Anti-VEGF

09/2012, VA: CF

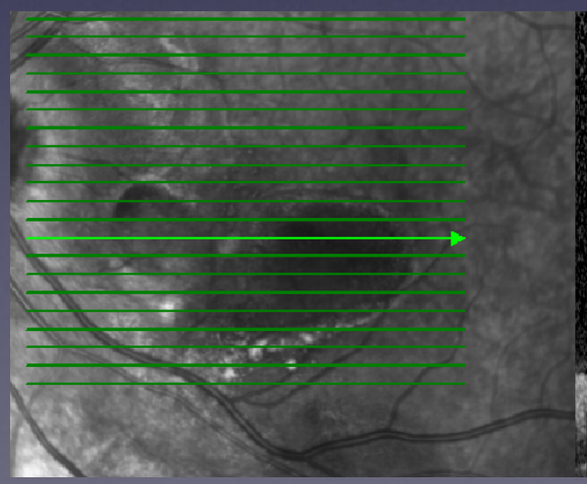


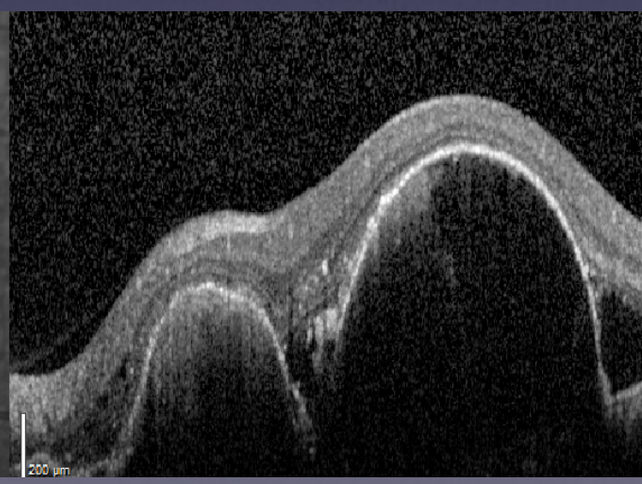




11/2012, VA: 0.4







01/2013: VA: 0.2

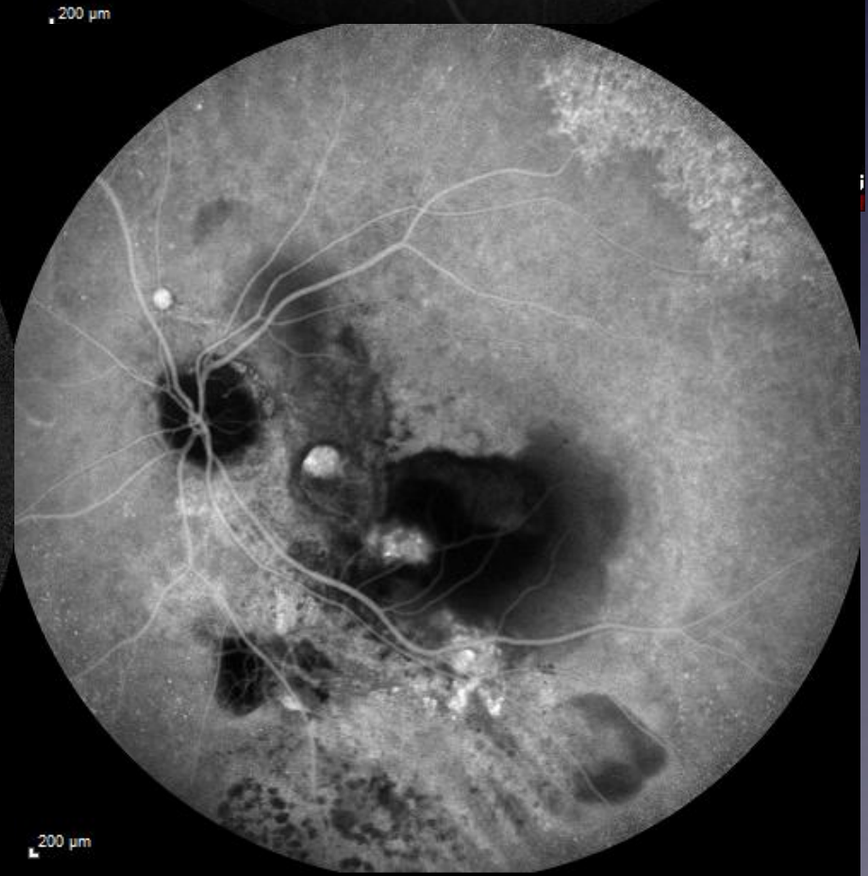






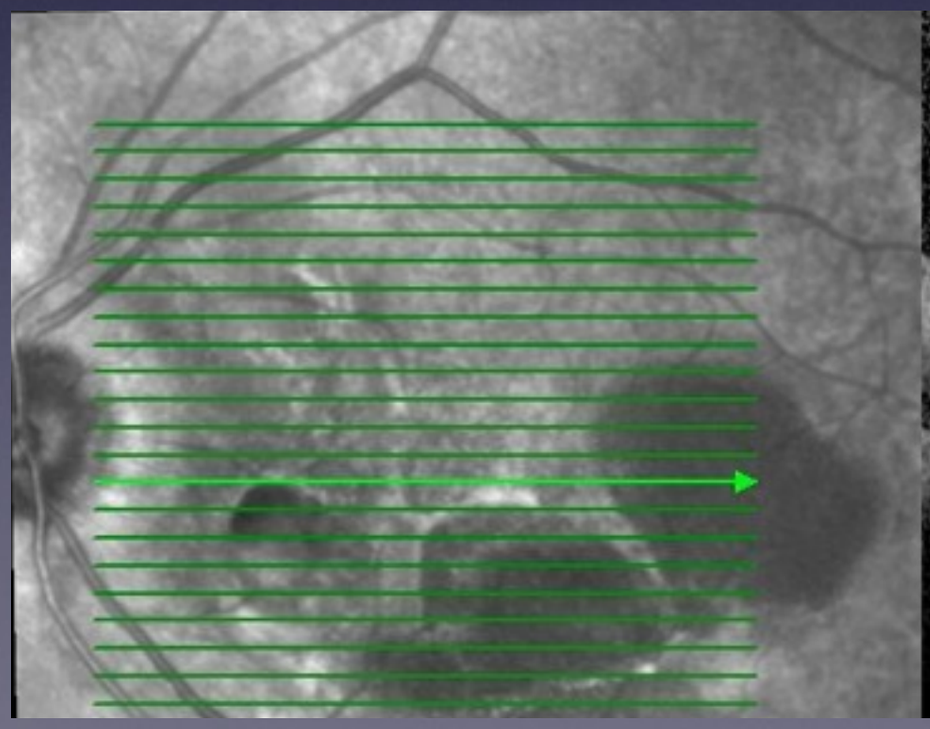
PDT+Anti-VEGF

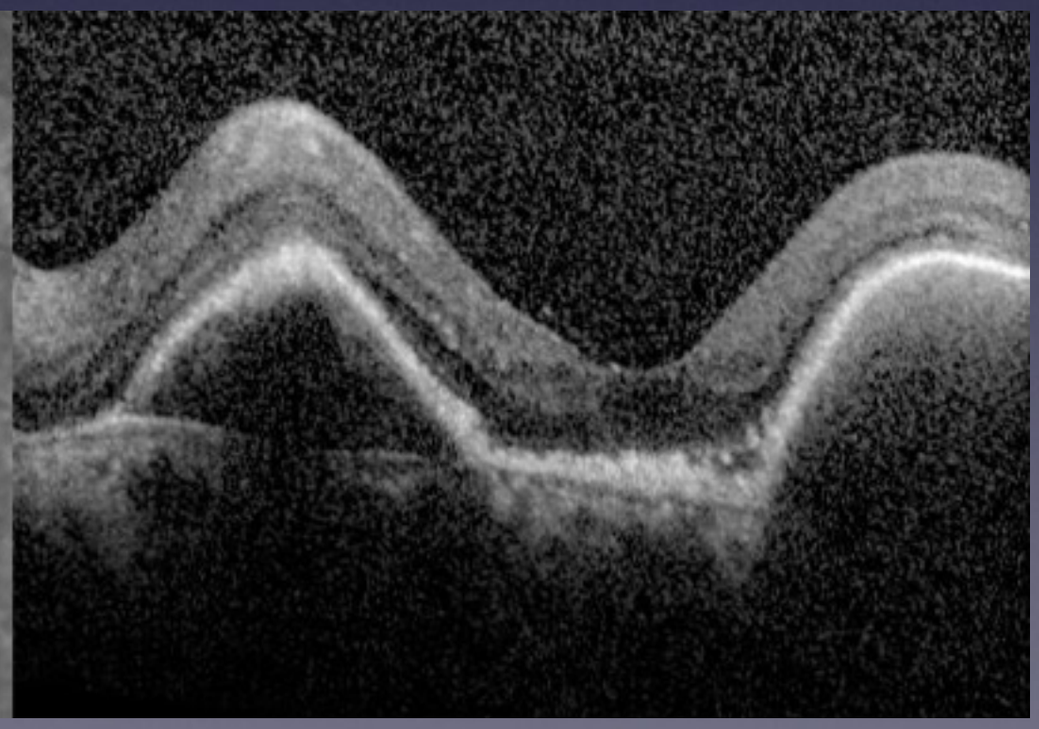




03/2013, VA: 0.3, IV Anti-VEGF

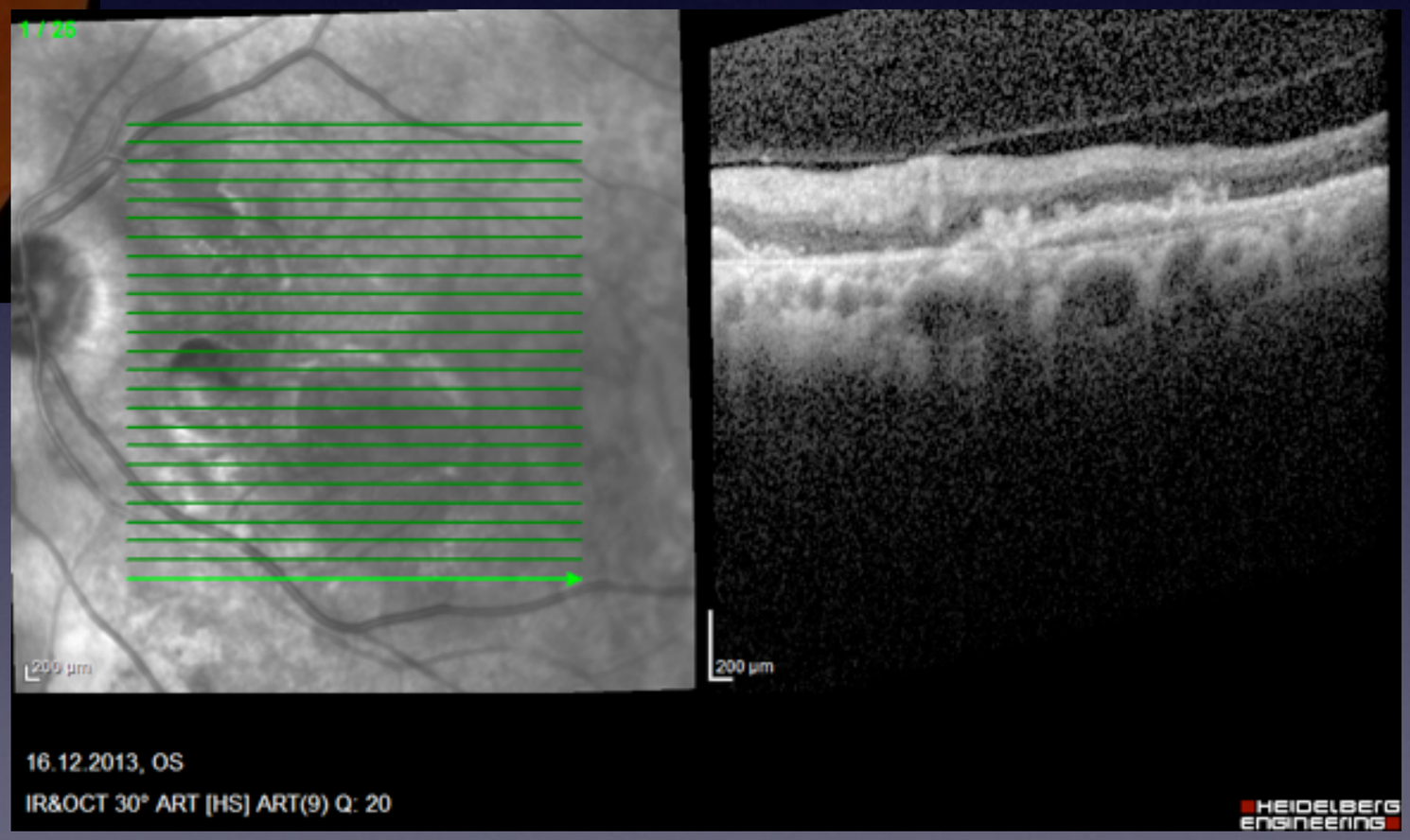






12/2013, VA: 0.2





2x PDT + 7 Anti-VEGF

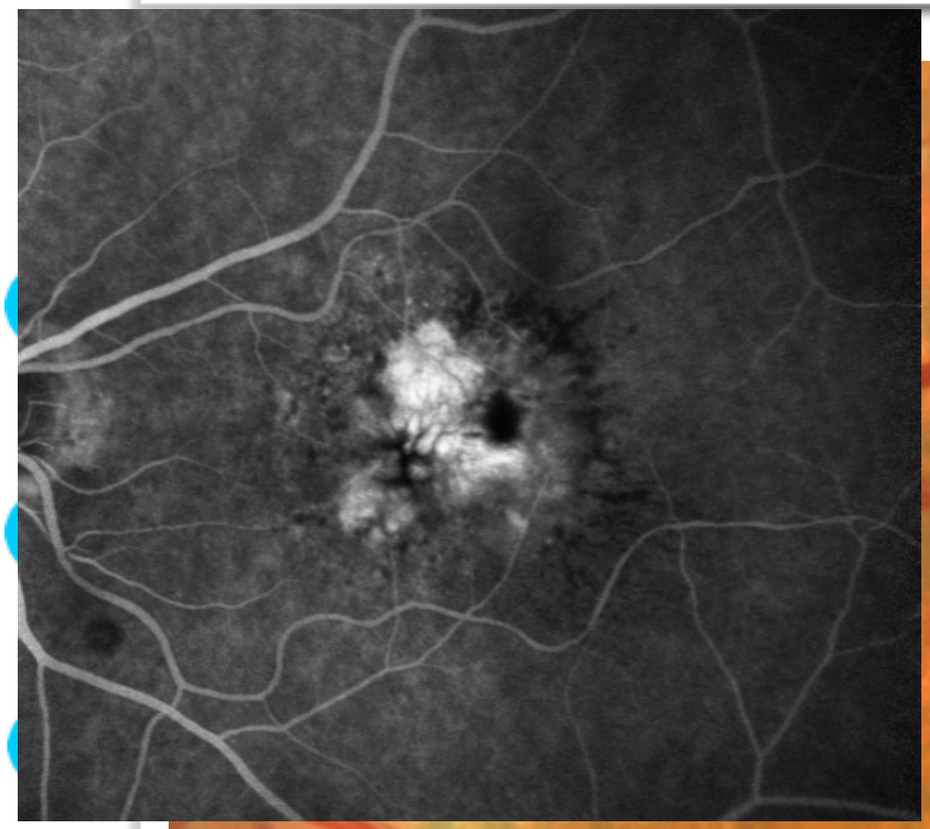
YANLIŞ TANI
RAP

- Yanuzzi 2001
- Tüm yaş tip YBMD %15'i (beyaz ırk), %4.5 (asyalı)
- Evre 1: İntraretinal neovaskülerizasyon
- Evre 2: Subretinal neovaskülerizasyon
- Evre 3: Klinik KNV

YANLIŞ TANI
RAP

- Tip 3 KNV
- Tedaviye daha dirençli
- Kombine tedaviler?
    - PDT
    - Steroidler
    - Anti-VEGF

RAP



YANLIŞ TANI

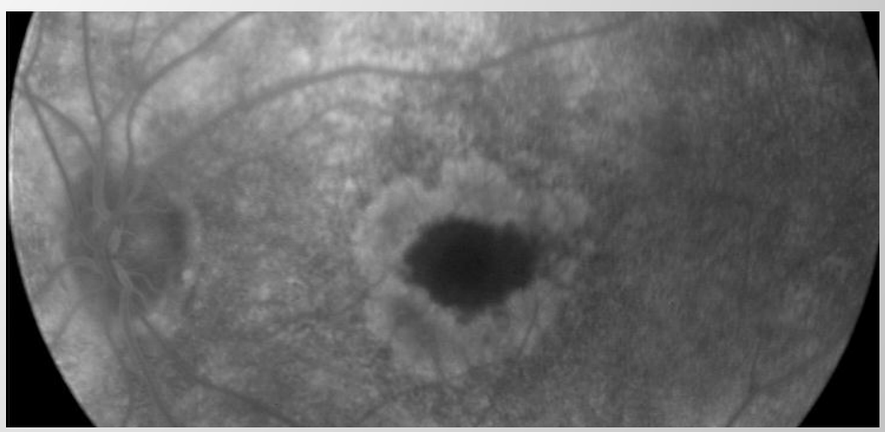
VİTELLİFORM LEZYONLAR

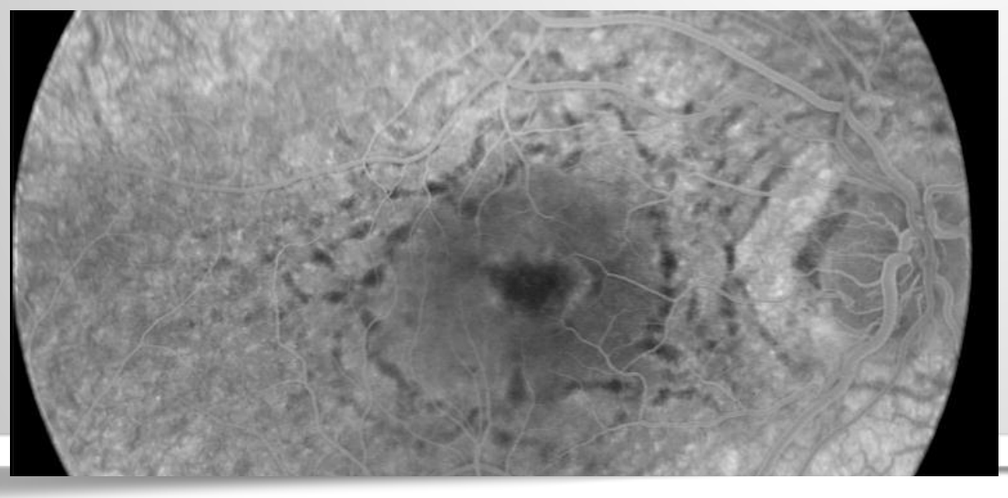
- PATERN DİSTROFİ



- AOVMD

- KELEBEK ŞEKİLLİ
- FUNDUS PULVERULENTUS





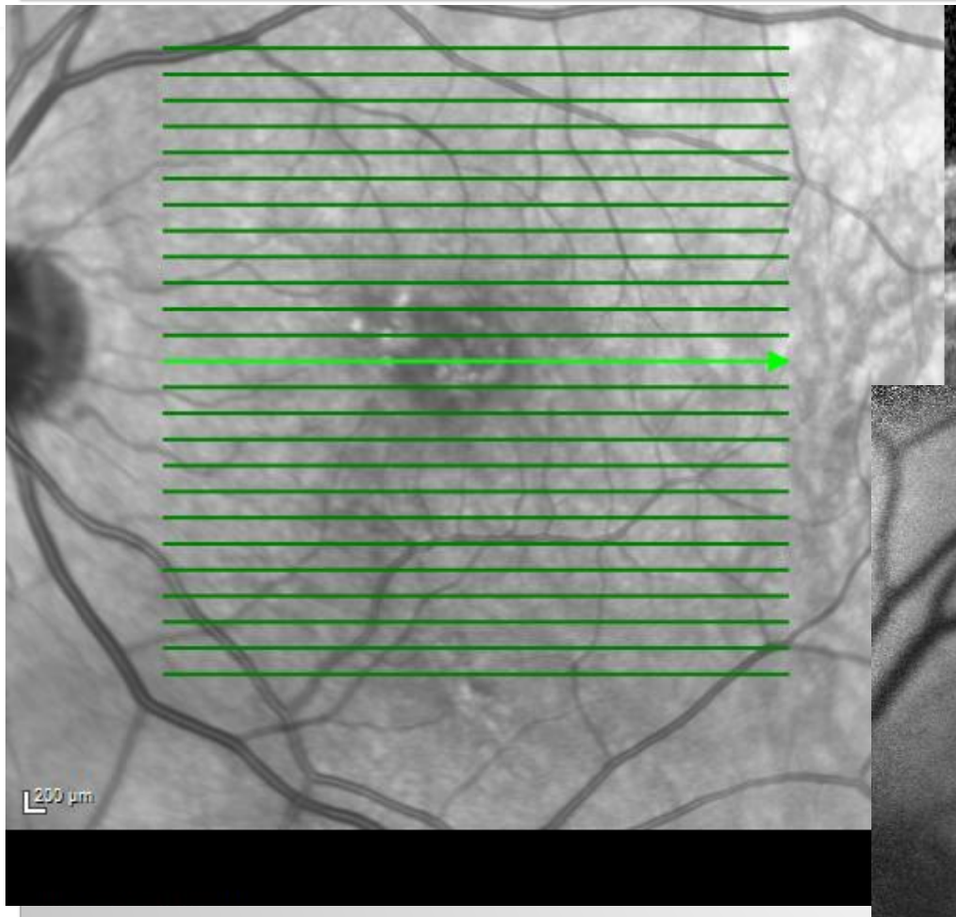
YANLIŞ TANI

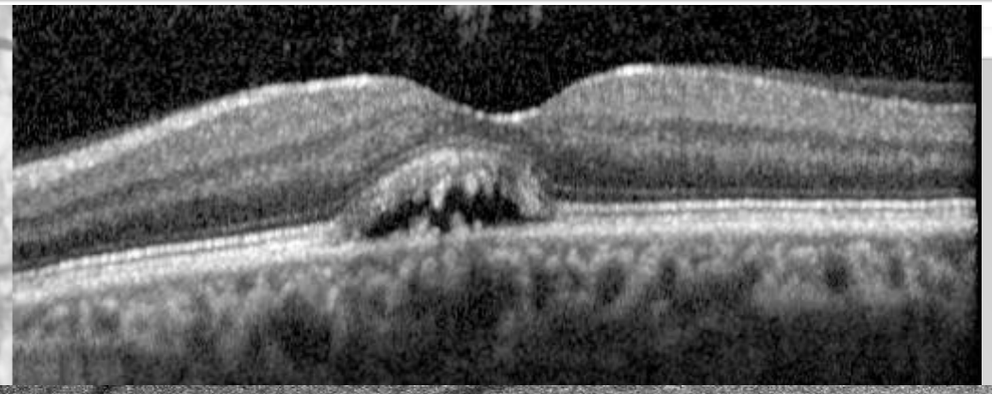
VİTELLİFORM LEZYONLAR-AOVMD

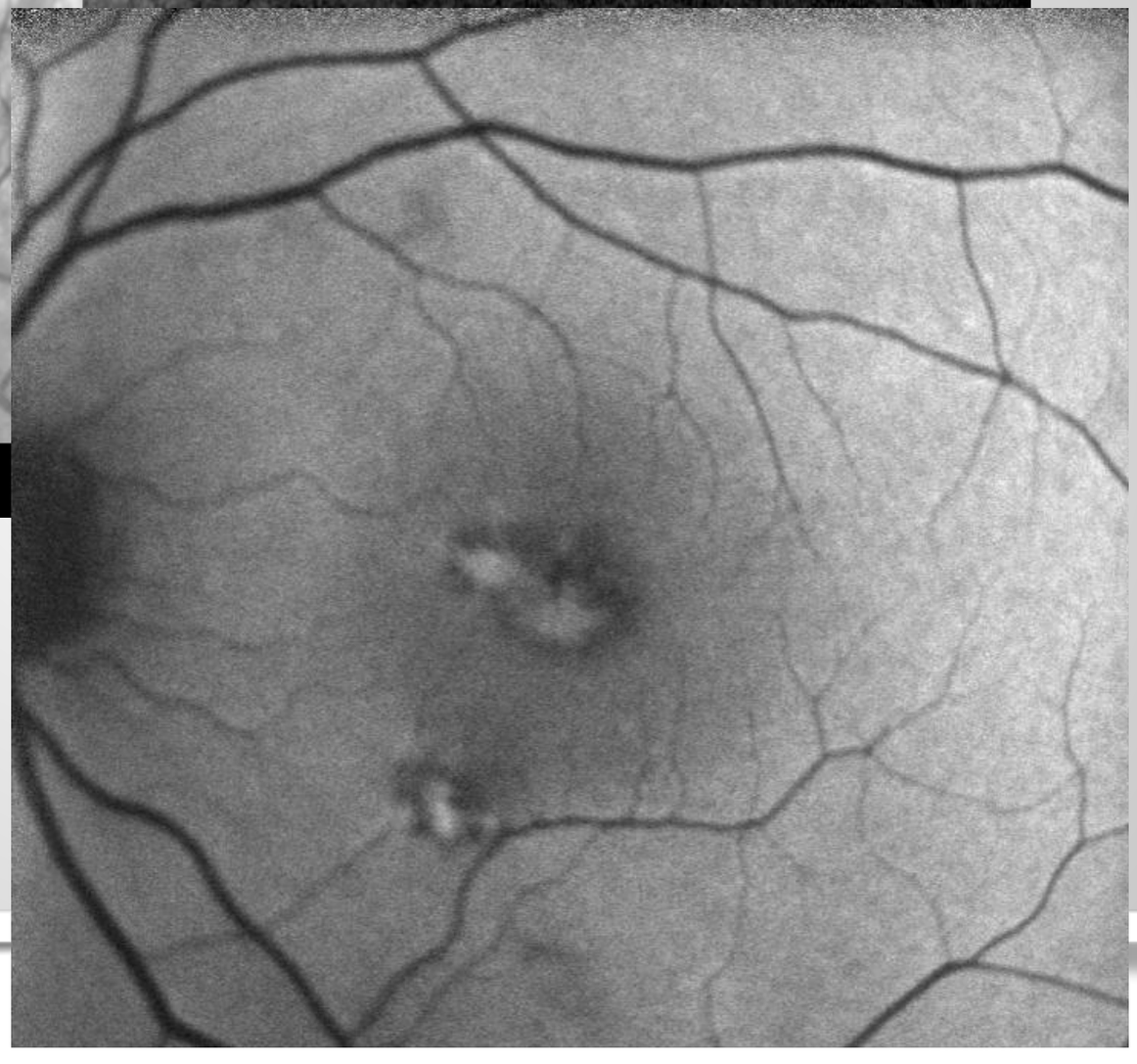


YANLIŞ TANI

AOVMD



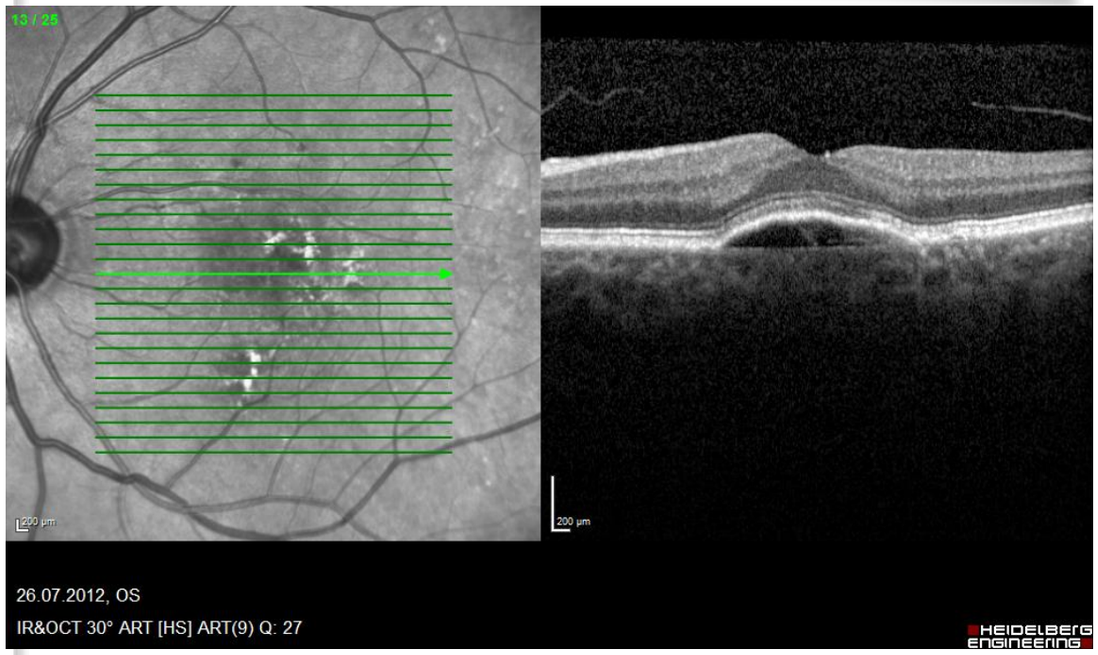


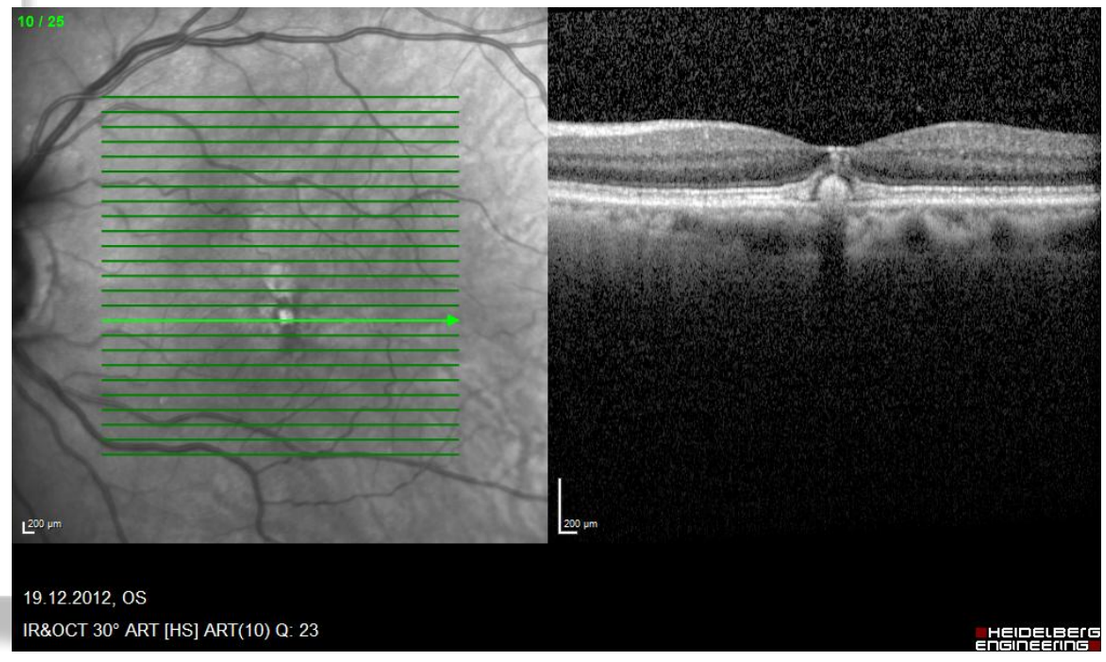


YANLIŞ TANI

VİTELLİFORM LEZYONLAR-**AOVMD**

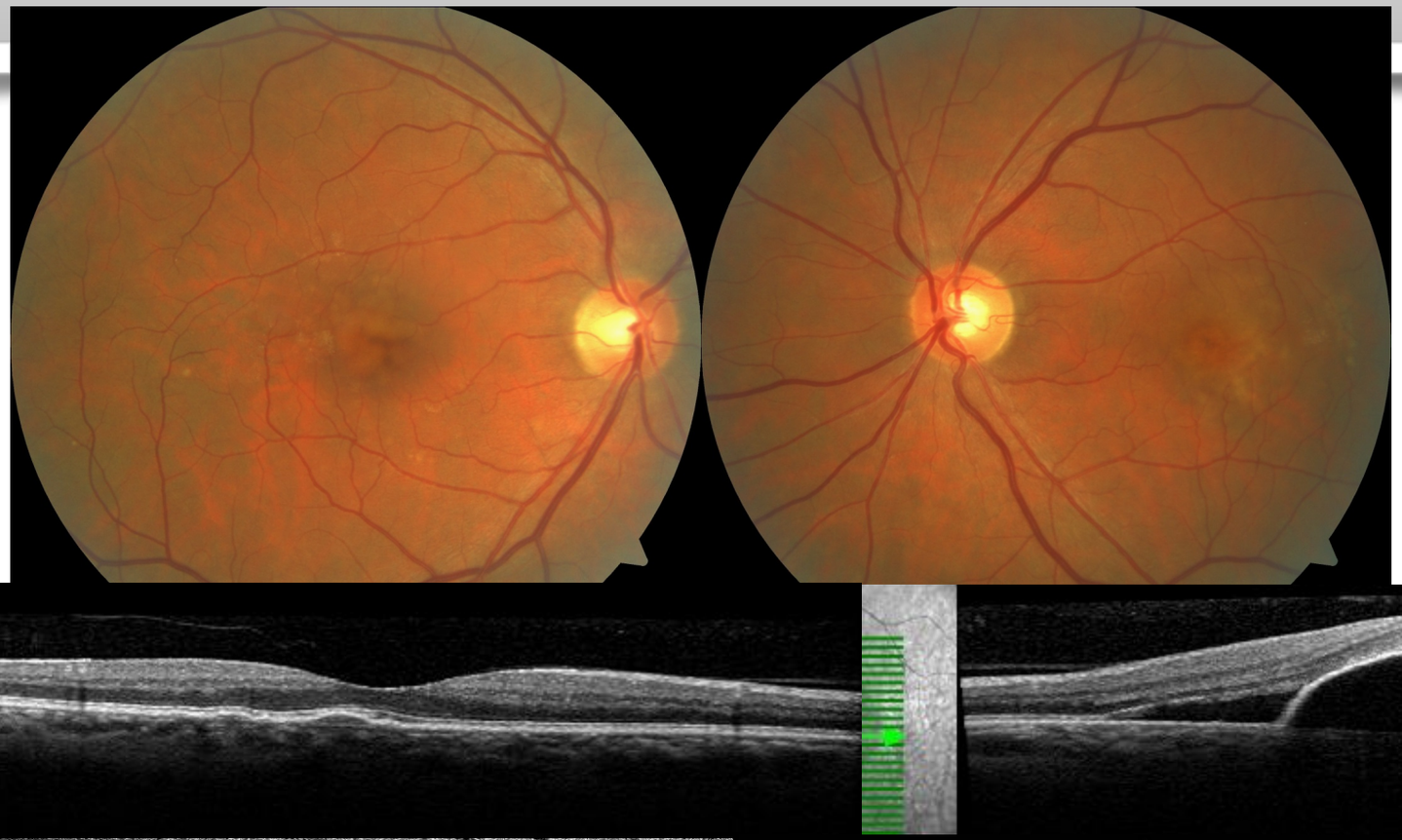
- Görme Düzeyi iyi
- Şikayetleri yok (min metamorfopsi)
- Tesadüfen farkedilir
- İntraretinal/subretinal sıvı yok
- Enjeksiyon yapılmış/ önerilmiş olabilir
- Daha seyrek KNV gelişebilir

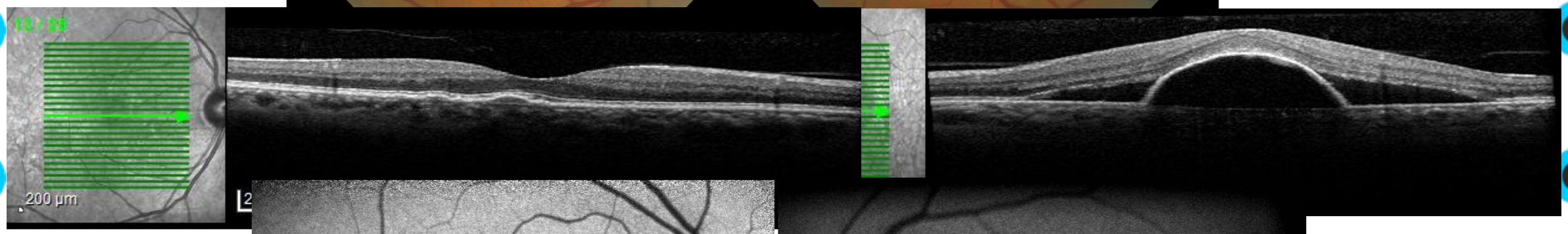




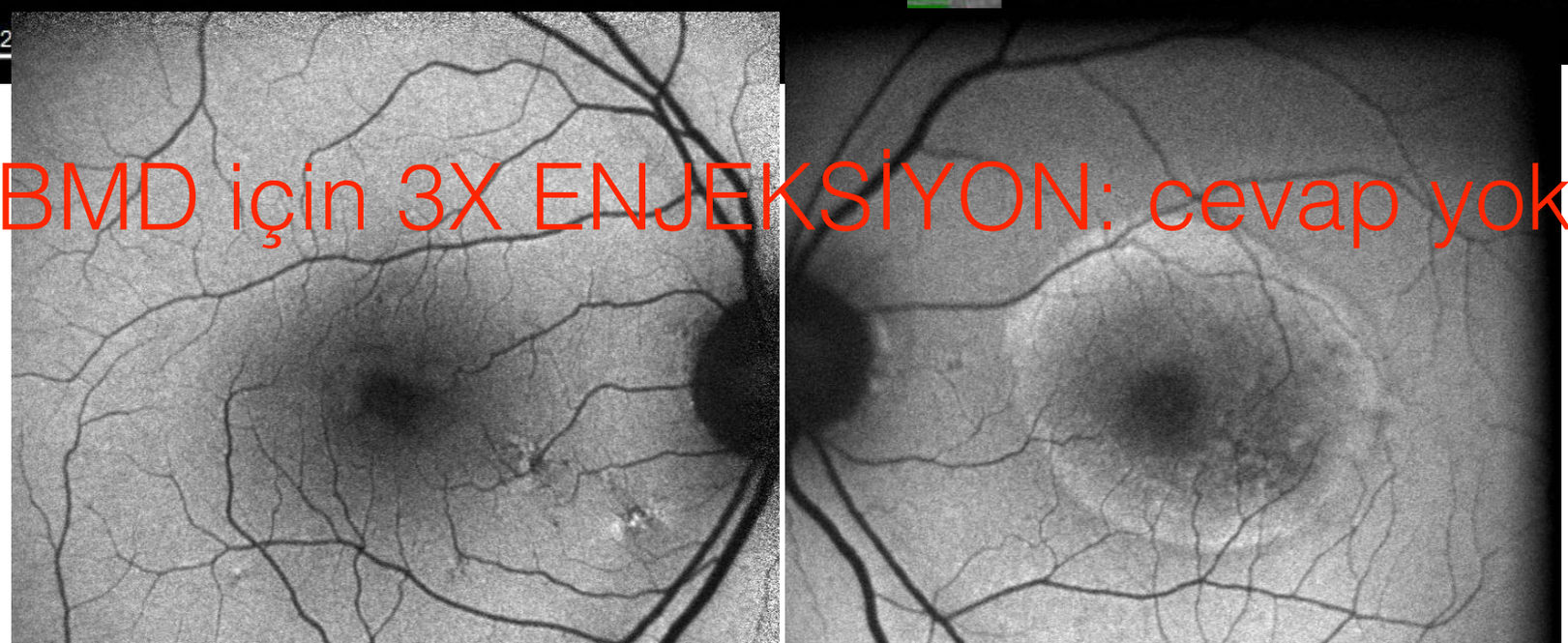
YANLIŞ TANI: SSKR

62y, K,
KG: 1.0/0.7



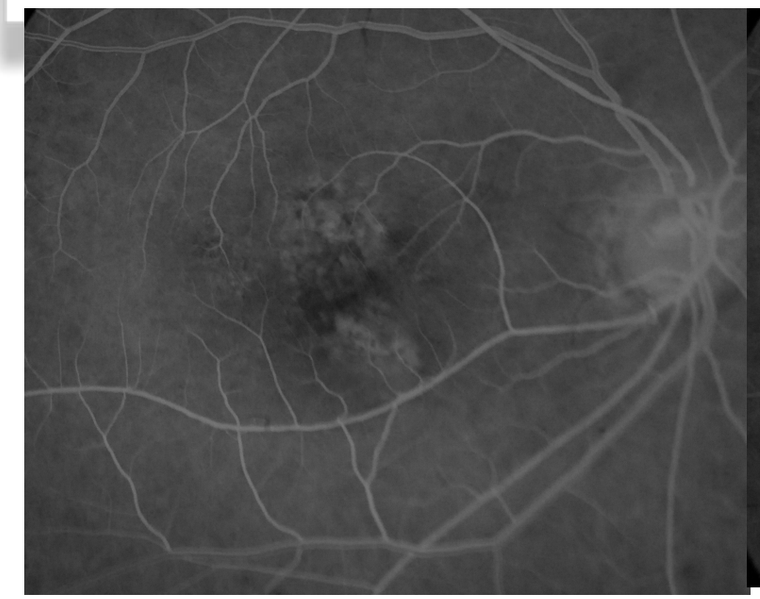


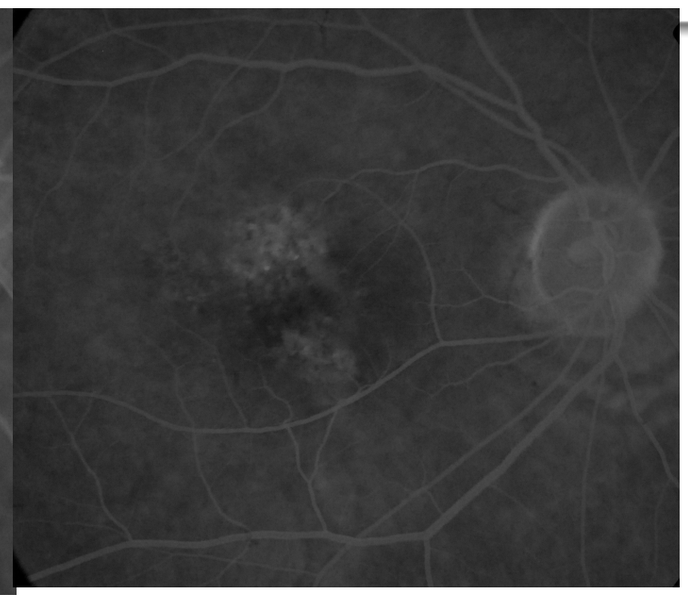
YBMD için 3X ENJEKSİYON: cevap yok!

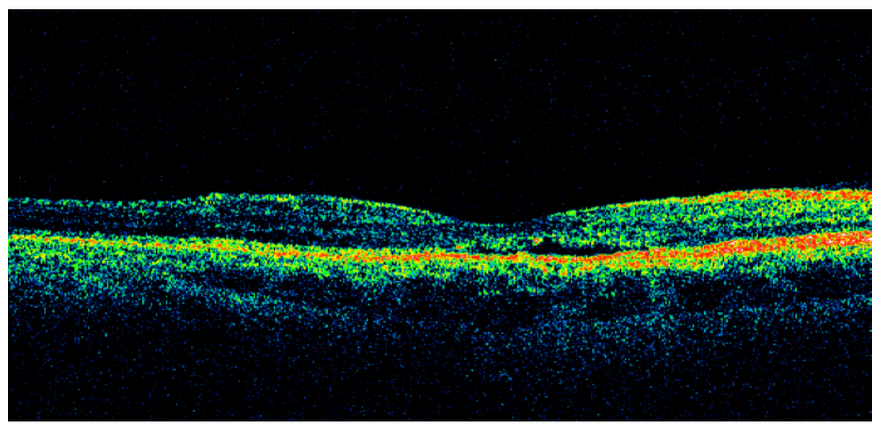


SSKR

55y, E, GK: 0.5

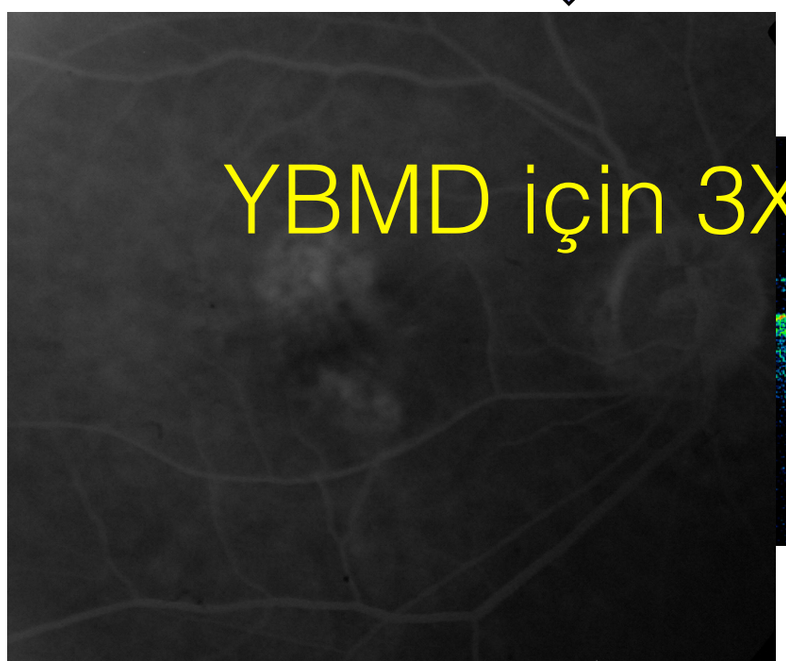


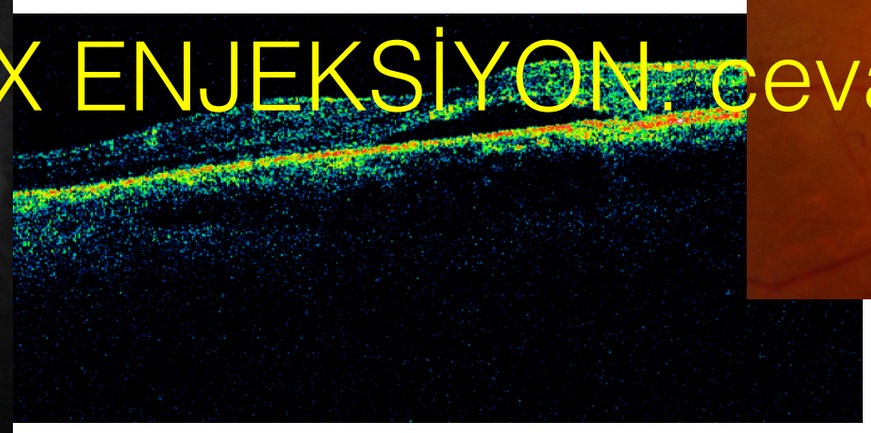




3X lucentis

GK: 0,5

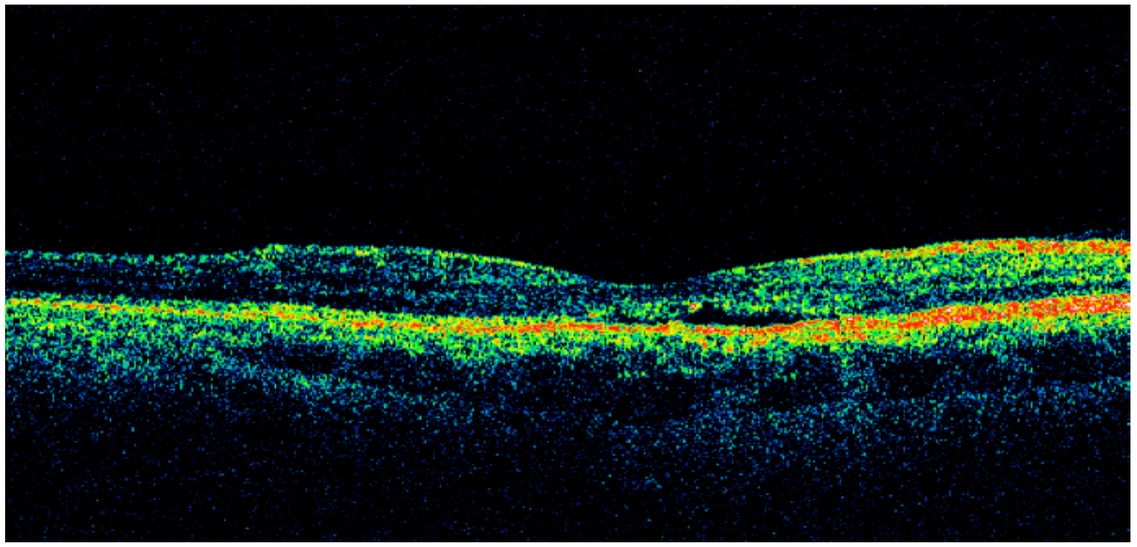




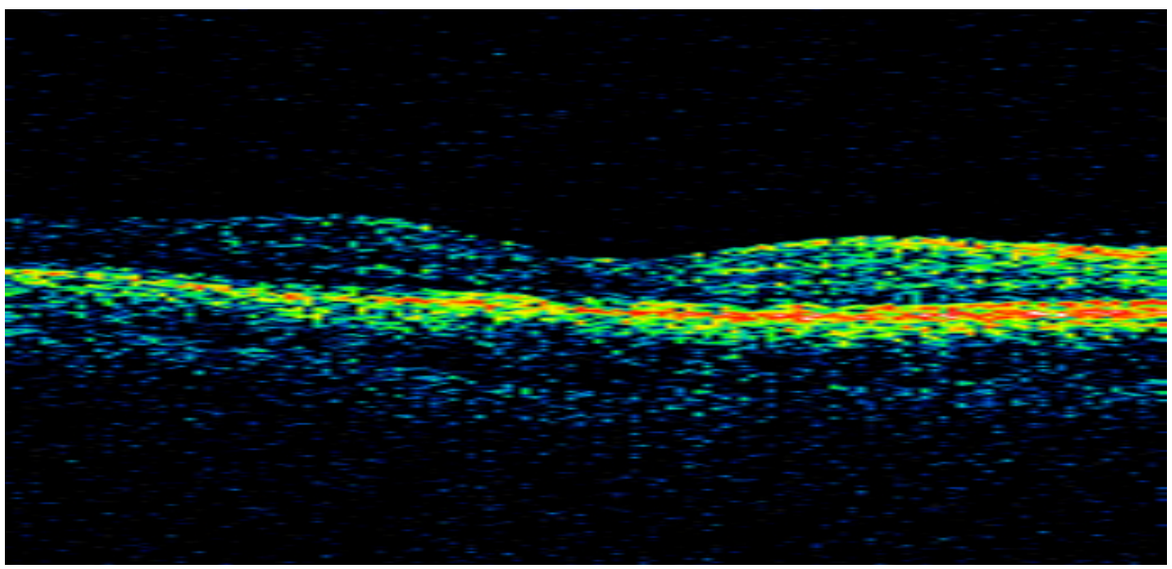
YBMD için 3X ENJEKSİYON: cevap yok!



SSKR



1/2 fluence PDT: 1. AY: GK: 0.7

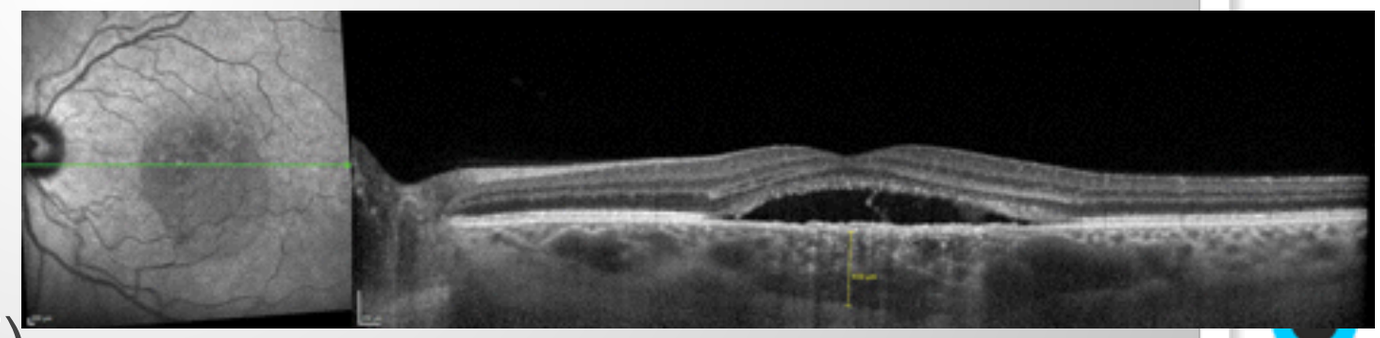


13.ay: GK: 0.8

YANLIŞ TANI

KRONİK SSKR

- Drusen yok!
- FA: Genellikle bilateral multiodaklı sızıntılar,
- OCT: Subfoveal sıvı ve PED (intraretinal sıvı -)
- ICG: Koroidal hyperpermiabilite
- EDI-OCT: Kalın koroid
- KVNM seyrek (Anti-VEGF)
- Tedavi: PDT



ANTİ-VEGF TEDAVİDE DİRENÇ

- YANLIŞ TANI (%46.2)

  -PCV, RAP, VİTELLİFORM, SSKR

- TAŞİFLAKSİ-TOLERANS (%22)
- CEVAPSIZLAR (%26.9)
- HEMORAJİK CEVAP
- KOMPLİKASYONLAR: RPE yırtığı, atrofi, skar oluşumuna bağlı görme kaybı (%11.6)

Manoj SM. Why does anti-VEGF treatment fail in AMD. Kerala Journal of Ophthalmology. 2011.

GEÇ DÖNEMDE AZALAN CEVAP… DİRENÇ?

Biyolojik ilaçların uzun süre kullanımı sonrası

etkinlikte progresif azalma

Taşiflaksi / Tolerans

TAŞİFLAKSİ

- Keane PA, Liakopoulos S, Ongchin SC, Heussen FM, Msutta S, Chang KT et al. Quantitative subanalysis of optical coherence tomography after treatment with ranibizumab for neovascular age-related macular degeneration. Invest Ophthalmol Vis Sci 2008; 49(7):3115-3120.

- Schaal S, Kaplan HJ, Tezel TH. Is there tachyphylaxis to intravitreal anti-vascular endothelial growth factor pharmacotherapy in age-related macular degeneration? Ophthalmology 2008; 115(12): 2199-2205.

- Forooghian F, Cukras C, Meyerle CB, Chew EY, Wong WT. Tachyphylaxis after intravitreal bevacizumab for exudative age-related macular degeneration. Retina 2009; 29(6):723-731.

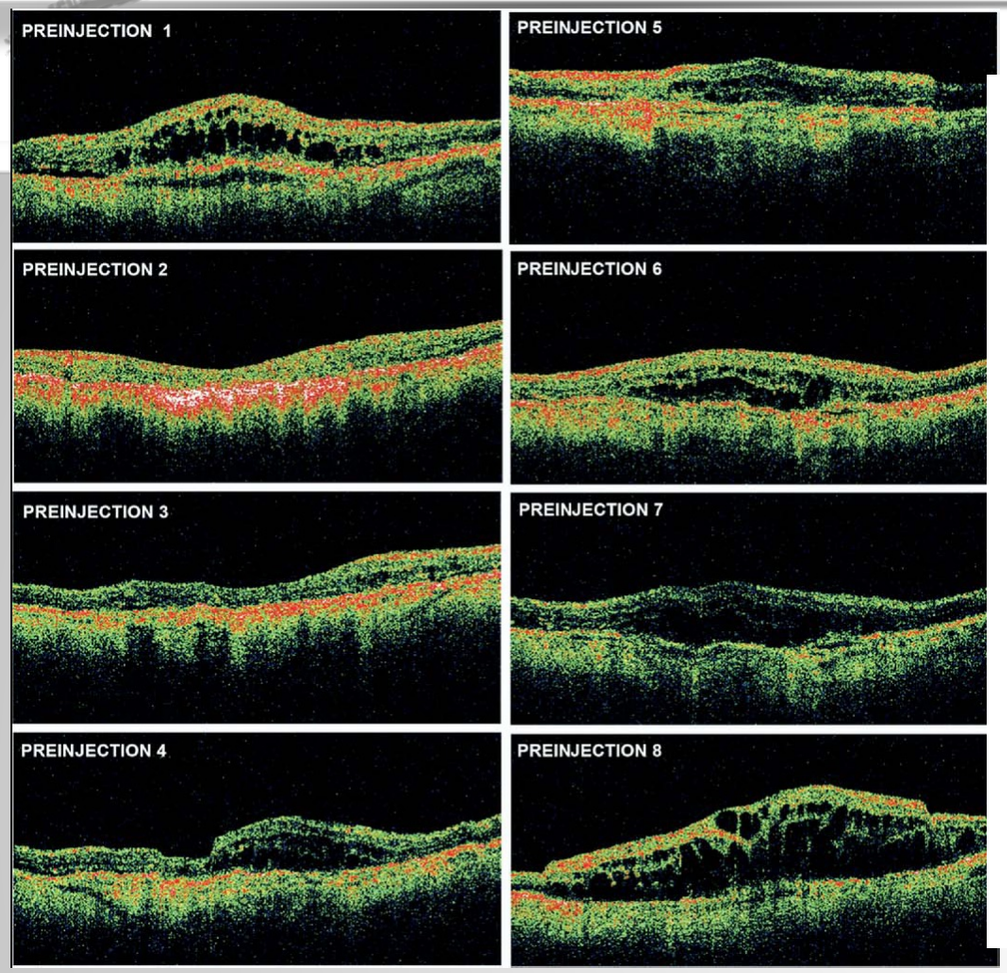
- Eghoj MS, Sorensen TL. Tachyphylaxis during treatment of exudative age-related macular degeneration with ranibizumab. Br J Ophthalmol 2012; 96(1):21-23.

- Gasperini JL et al. Bevacizumab and ranibizumab tachyphylaxis in the treatment of choroidal neovascularisation. Br J Ophthalmol. 2012

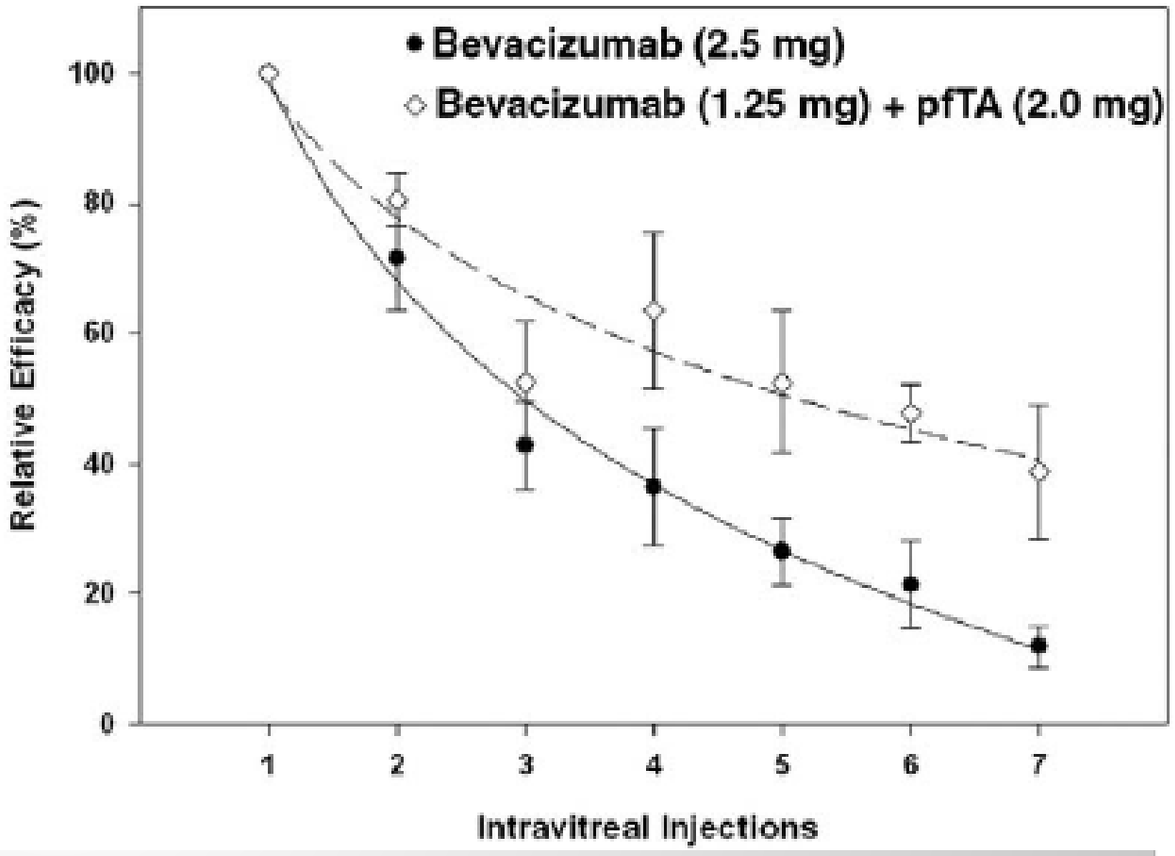
- Tranos P et al. Resistance to anti-VEGF treatment in AMD.Drug Design, Development and Therapy 2013 (Review)

- Binder S. Loss of reactivity in intravitreal anti-VEGF therapy: tachyphylaxis or tolerance? Br J Ophthalmol 2012; 96(1):1-2. (editorial)

TAŞİFLAKSİ



Biyoetkinlikte azalma!..



- Schaal S, Kaplan HJ, Tezel TH. Is there tachyphylaxis to intravitreal anti-vascular endothelial growth factor pharmacotherapy in age-related macular degeneration? Ophthalmology 2008; 115(12):2199-2205.

TAŞİFLAKSİ

Forooghian F et al. Tachyphylaxis Following Intravitreal Bevacizumab for Exudative ARMD. Retina 2009.

- NIH
- Taşiflaksi
- 6/59 göz: %10
- Ort 8 enjek, ort 100 hafta

Eghoj MS, Sorensen TL. Tachyphylaxis during treatment of exudative age-related macular degeneration with ranibizumab. Br J Ophthalmol 2012; 96(1):21-23.

- Taşiflaksi
- 20/1076 göz: (%2)

TAŞİFLAKSİ

- Doheny Eye Institute
- 26 gözde taşiflaksi
- Bazıları 2-3 enjeksiyon, bazıları 10-11 enjeksiyon sonrası
- %81'i diğer anti-VEGF'e geçiş ile bir miktar olumlu cevap

- Gasperini JL et al. Bevacizumab and ranibizumab tachyphylaxis in the treatment of choroidal neovascularisation. Br J Ophthalmol. 2012

GEÇ DÖNEMDE AZALAN CEVAP

- Erken (2-3 enjeksiyon sonrası): Taşiflaksi
- Geç (10-15 enjeksiyon sonrası): Tolerans

- Binder S. Loss of reactivity in intravitreal anti-VEGF therapy: tachyphylaxis or tolerance? Br J Ophthalmol 2012; 96(1):1-2.
- Schaal S, Kaplan HJ, Tezel TH. Is there tachyphylaxis to intravitreal anti-vascular endothelial growth factor pharmacotherapy in age-related macular degeneration? Ophthalmology 2008; 115(12):2199-2205.

GÜTF Çalışma-Amaç

Tachyphylaxis during ranibizumab treatment of exudative age–related macular degeneration

Sibel Doguizi[1], Sengul Ozdek[2], Selcen Yuksel[3]

Int J Ophthalmol, 2015

- Neovasküler YBMDnin anti-VEGF lerle tedavisi sırasında taşiflaksi-tolerans gelişme oranları
- Taşiflaksi-tolerans gelişen hastaların klinik özelliklerini belirlemek

Hastalar ve Method

- Retrospektif çalışma: Neovasküler YBMD için anti-VEGF tedavisi alan hastaların dosyalarının incelenmesi
- OCT hacimlerinin kantitatif analizi
- Tekrarlayan enjeksiyonların retinal hacmi azaltmadaki etkinliğinin azalması

Tanım

- Erken pozitif cevap (SFK veya PED yüksekliğinde azalma)
- Sonradan enjeksiyonlara rağmen tedaviye cevabın giderek azalması (SFK veya PED yüksekliğinde artış)
- Tedavi ile SFK veya PED yüksekliğinde stabilizasyon taşiflaksi/tolerans olarak kabul edilmemiştir.

- Olumsuz cevabın gelişimi:
  - <6 enjeksiyon: Taşiflaksi
  - ≥6 enjeksiyon: Tolerans

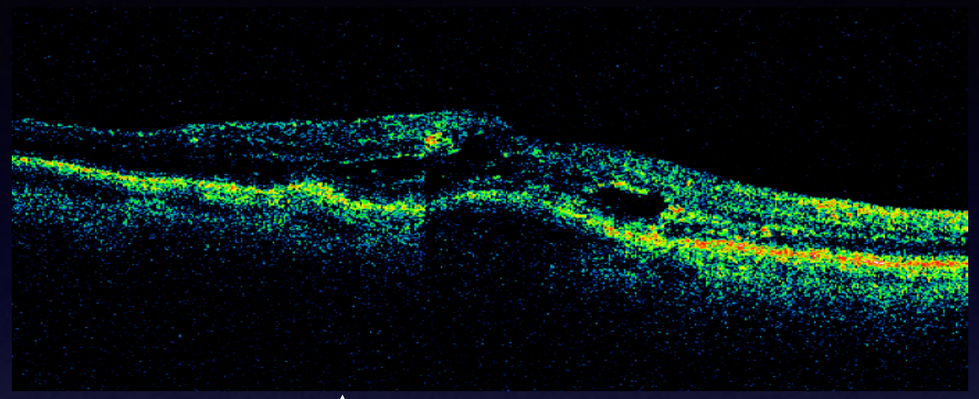
Bulgular

- 206 göz (201 hasta)
- Toplam 16 gözde tedaviye cevapta azalma görüldü (%7.7)
- Ortalama takip: 49.5 ay (36-63 ay)
- Taşiflaksi 12 göz (%5.8)
- Tolerans 4 göz (%1.9)
- Gizli KNV:10 göz (%62.5)
- Predominant Klasik KNV: 6 göz (%37.5)

Medyan enjeksiyon sayısı

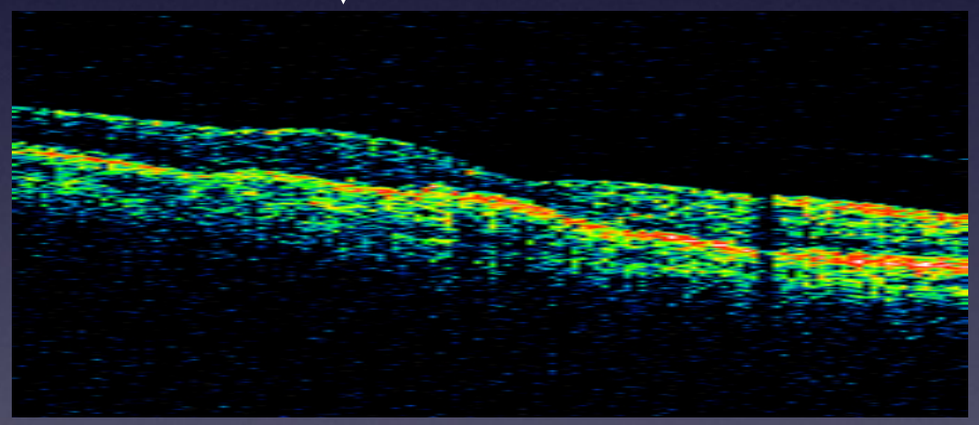
- Taşiflaksi gelişene kadar: 3.5 (2-5)
- Tolerans gelişene kadar: 11 (7-21)

Olgu 1: 64y / K



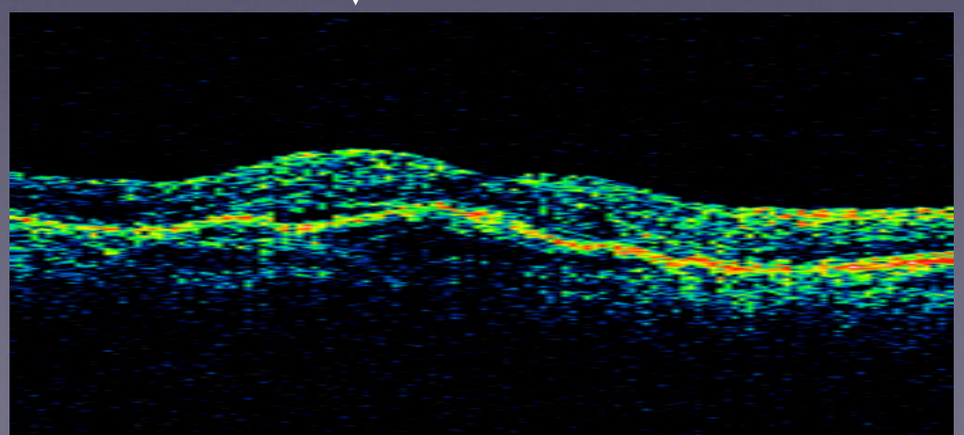
VA: 0.3

3x Lucentis



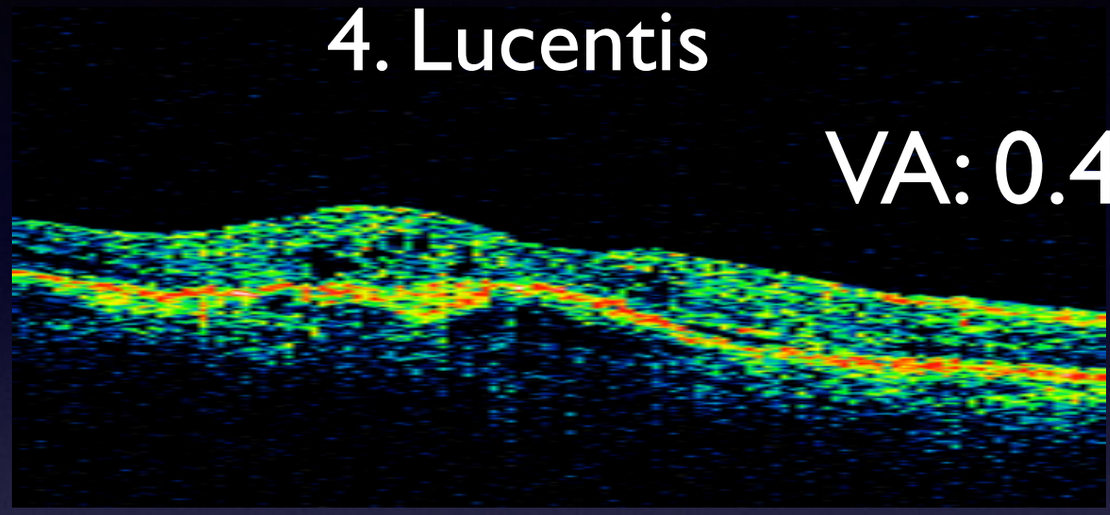
VA: 0.5

2 ay



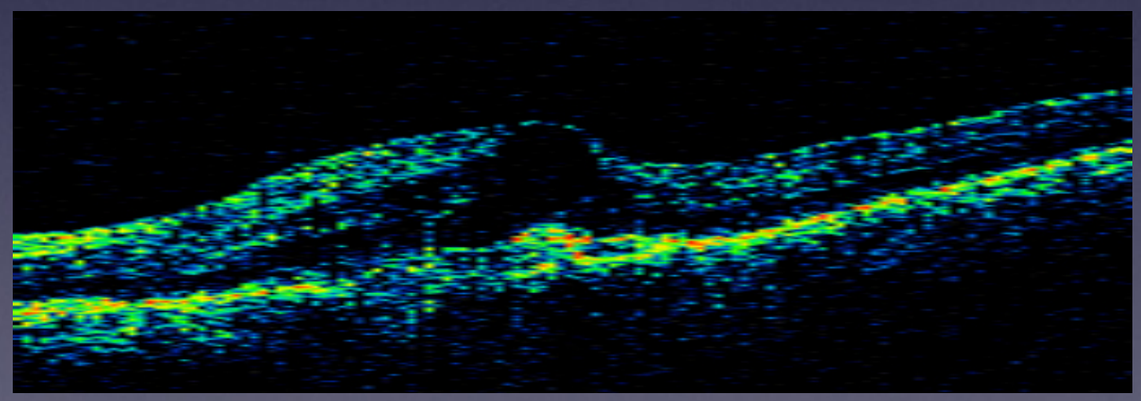
VA: 0.3

4. Lucentis



VA: 0.4

3x Lucentis



10.ay: VA: 0.2

MEKANİZMALAR

- Uzun sureli kullanımda reseptörlerin desensitizasyonu (tolerans)
    - Çözüm: Daha sık veya daha yüksek doz tedavi?
    - Forooghian et al: high-dose IVB (2.50 mg) did not restore the therapeutic response (Retina 2009)
- Farmakodinamik Tolerans: Artmış VEGF Expresyonu (Daha sık veya daha yüksek doz tedavi)
- Sistemik immün cevap (nötralizan antikorlar): *Farmakokinetik Tolerance*
    - Schaal et al (Ophthalmology 2008): tachyphylaxis can be partially alleviated by the subsequent use of preservative-free triamcinolone

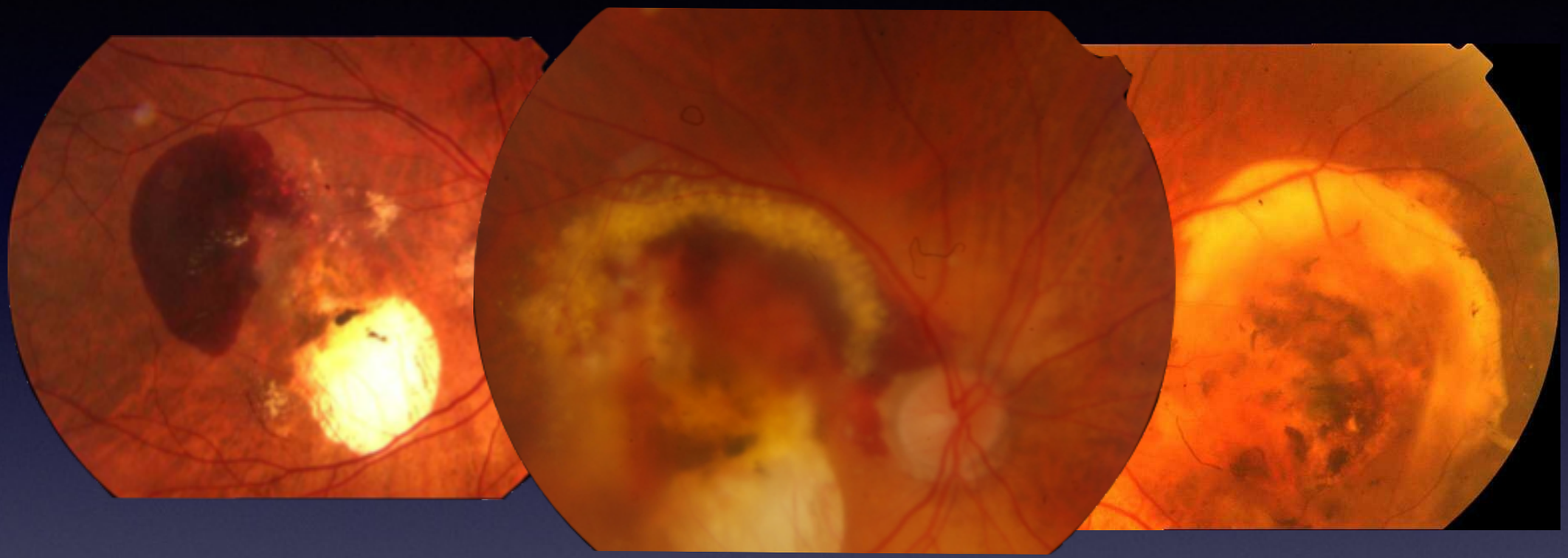
MEKANİZMALAR

- Diğer anjiojenik faktörlerde bloke VEGF'i kompanze etmek için artış (fibroblast GF, PlGF)
    - Aflibercept (VEGF-trap eye): blockage of another pathway "plasental growth factor (PlGF)": dramatic responses in eyes refractory to IVB&IVR (Patel et al Eye, 2013)
- Anormal damarların matürasyonu
- KNV de Fibrozis: Rezorbsiyon bariyeri

Çözüm Önerileri

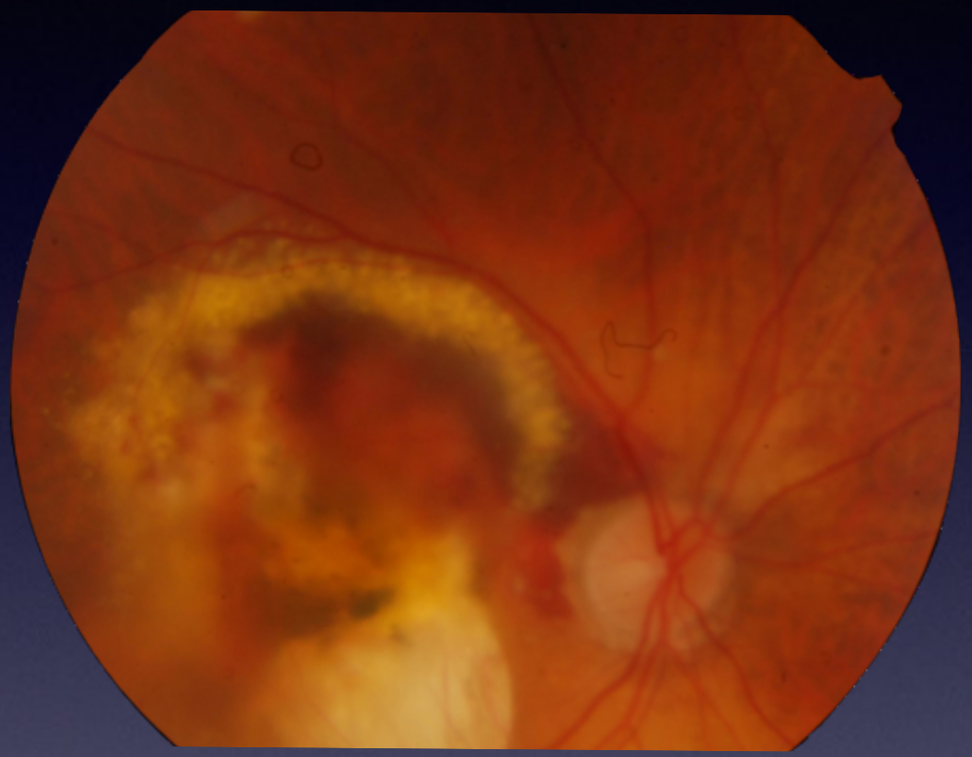
- Taşiflaksi:
  - Tedaviye ara vermek
  - Başka anti-VEGF'e geçiş
- Tolerans:
  - Dozu arttırmak,
  - Tedavi aralıklarını azaltmak,
  - Steroid eklemek
  - Başka anti-VEGF'e geçmek veya diğer yolakların blokajı (PlGF)

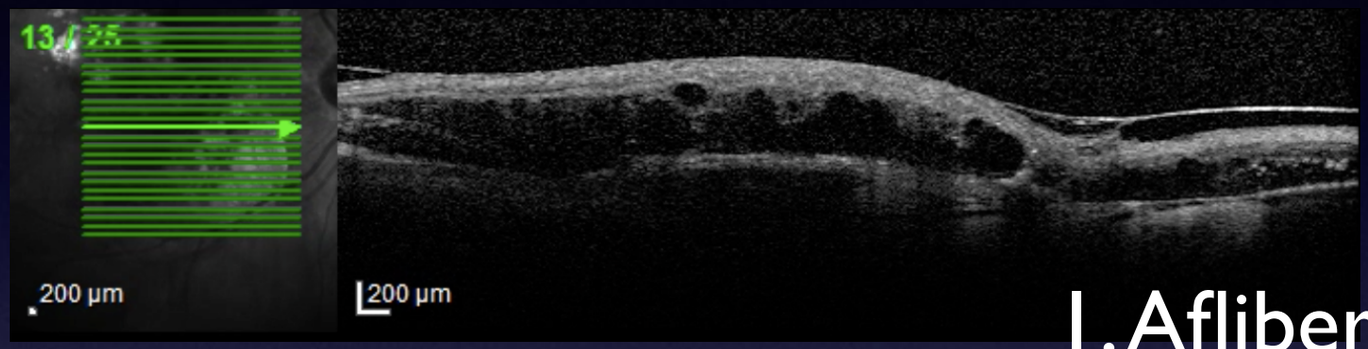
76y /K GK: 20/400 (R) EH (L)



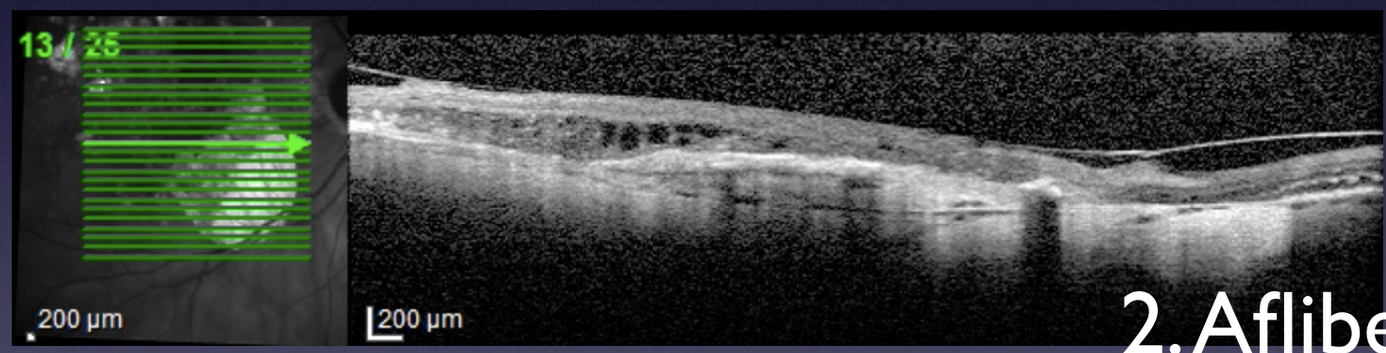
- 2007: 5x Avastin
- 2008: 6x Avastin
- 2009: 6x Lucentis
- 2010: 7x Lucentis
- 2011: 10x Lucentis, 2x IVTA
- 2012: 11x Lucentis
- 2013: 11x Lucentis

2014-Switch

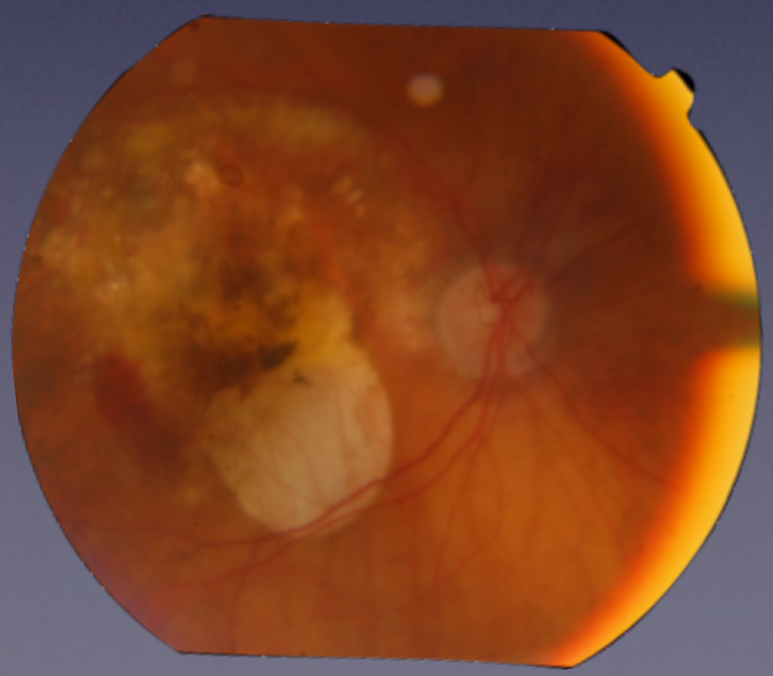


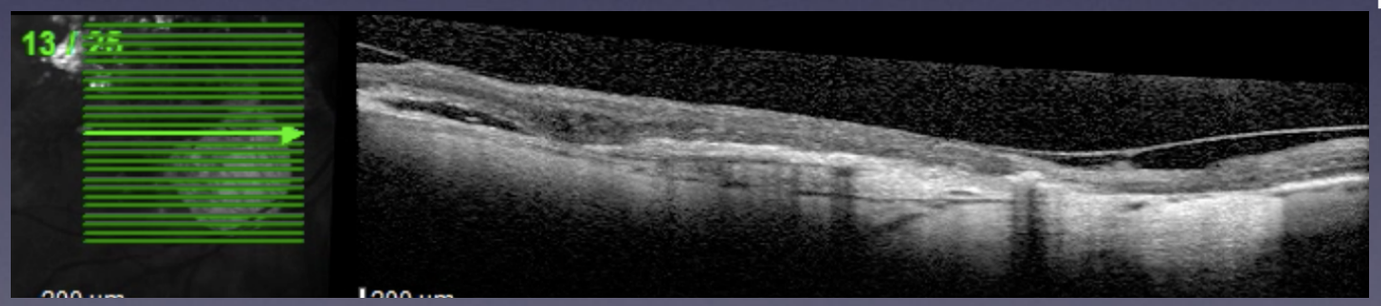


1. Aflibercept



2. Aflibercept





ANTİ-VEGF TEDAVİDE DİRENÇ

- YANLIŞ TANI (%46.2)

  -PCV, RAP, VİTELLİFORM, SSKR

- TAŞİFLAKSİ-TOLERANS (%22)

- CEVAPSIZLAR (%26.9) (İLK 3 DOZ İLE SIVI↑ VEYA GK↓ **AS!**)

- HEMORAJİK CEVAP

- KOMPLİKASYONLAR: RPE yırtığı, atrofi, skar oluşumuna bağlı görme kaybı (%11.6)

Manoj SM. Why does anti-VEGF treatment fail in AMD. Kerala Journal of Ophthalmology. 2011.

CEVAPSIZLIK

- YETERLİ VE DÜZENLİ AYLIK ENJEKSİYONLARA RAĞMEN!

- TAKİPLERDE OCT SIVI↑, GK↓, HEMORAJİ↑, LEZYON BÜYÜYORSA…… **AS↑**

- STABİL İSE (GK AYNI, SIVI AYNI, AS AYNI): CEVAPSIZ DENEMEZ!….AYNI TEDAVİYE DEVAM

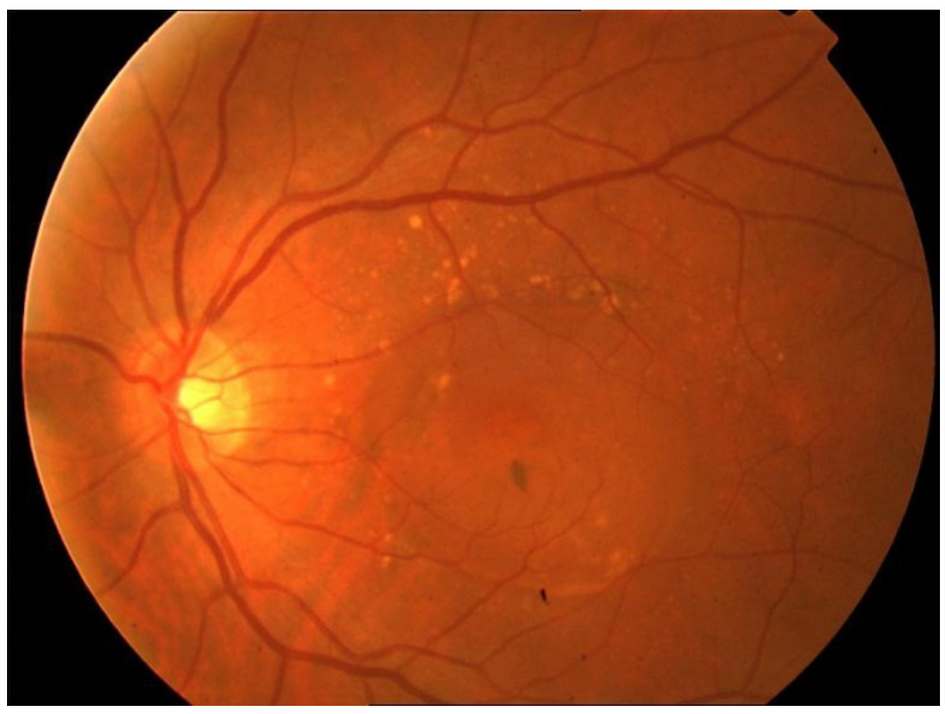
- GÖRME STABİL, SIVI AZALIYOR AMA (+): KISMİ CEVAP…..AYNI TEDAVİYE DEVAM

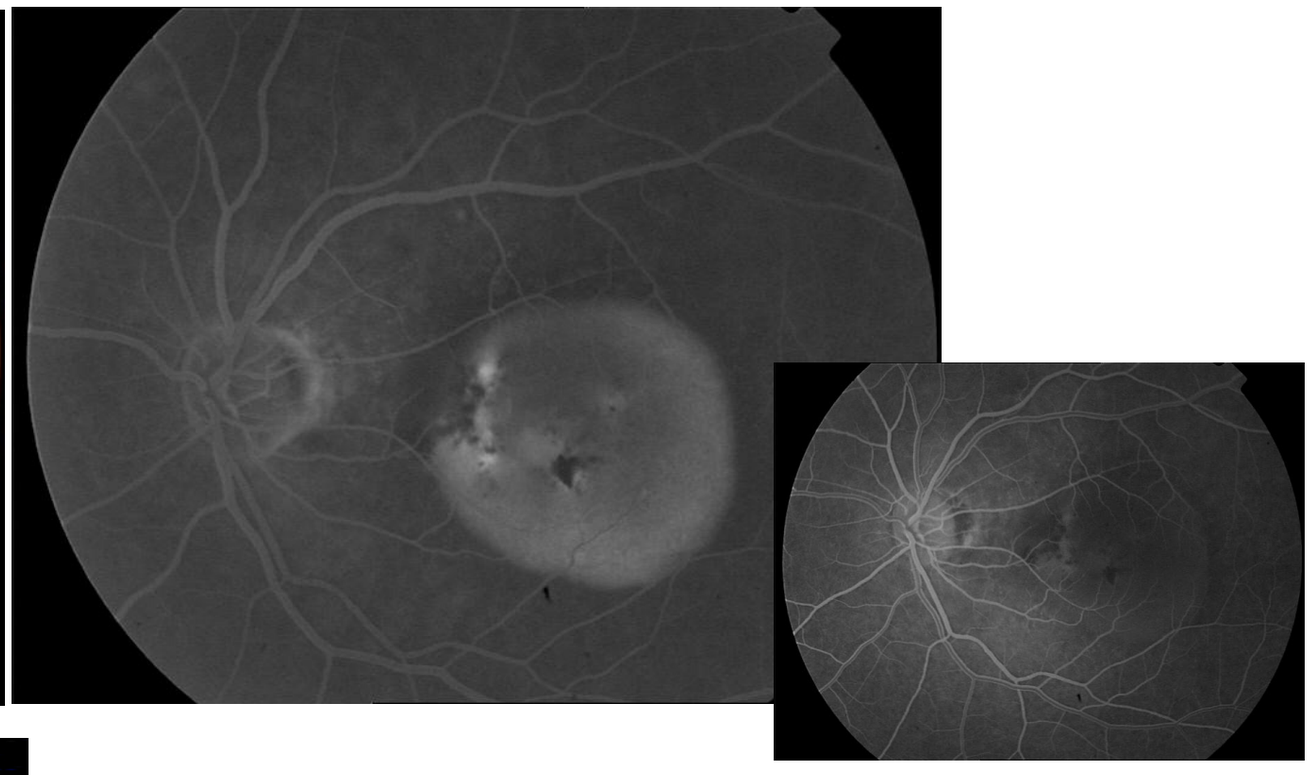
CEVAPSIZLIK

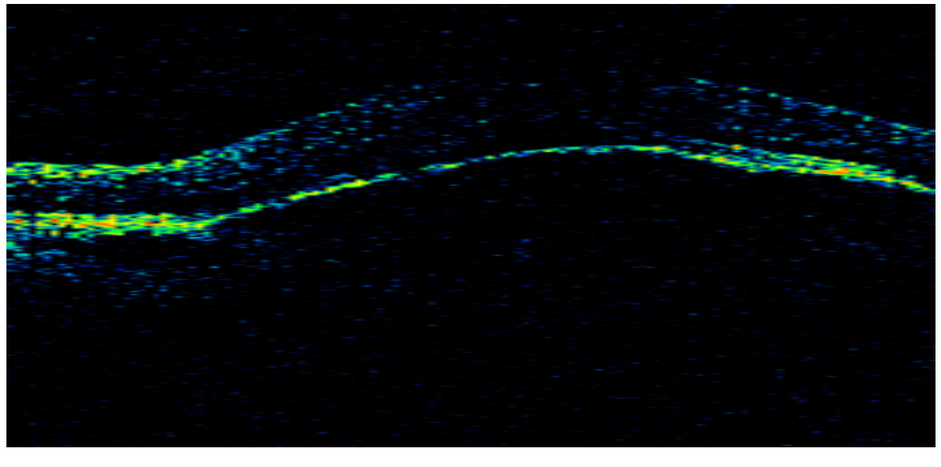
- KNV TİPİ (PCV, RAP)
- KNV MATURASYONU,
- GENETİK
- VMT-ERM VARLIĞI
  - Karaca EE, Kepez YB, Çubuk MÖ, Özdek Ş. Epiretinal membranes in neovascular age-related macular degeneration: effect on outcomes of anti-VEGF therapy. Retina. 2015

CEVAPSIZLIK

69Y, K, GK: 0.4

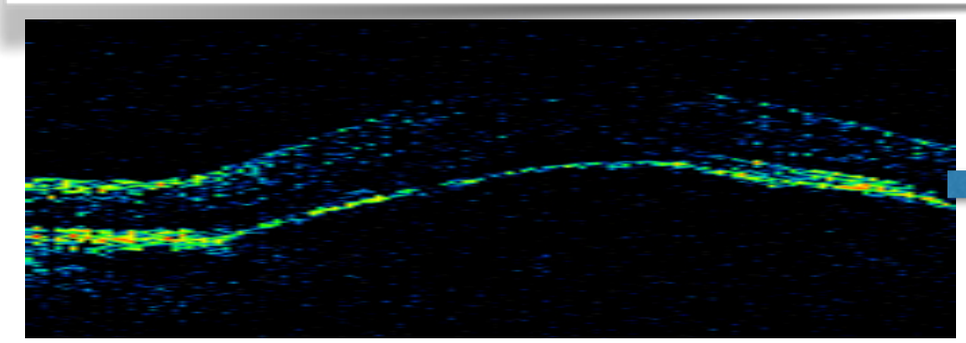


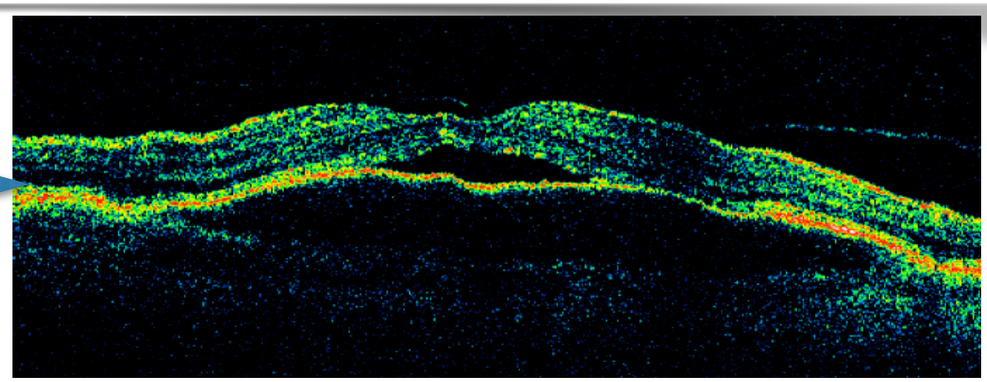




3X Avastin

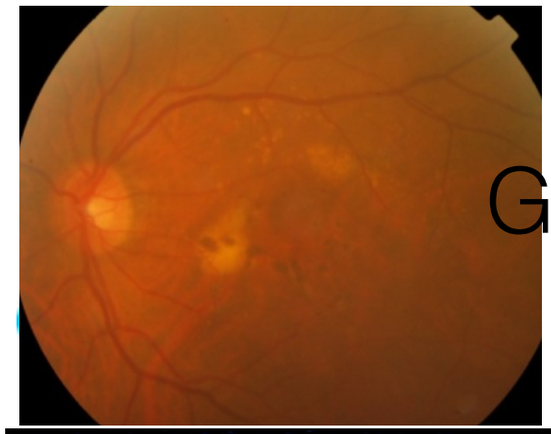
69Y, K, GK: 0.4



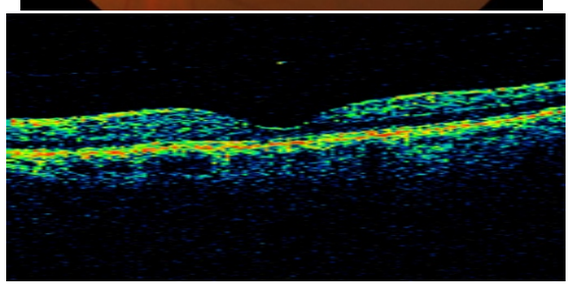


3X Avastin sonrası GK: 0.3

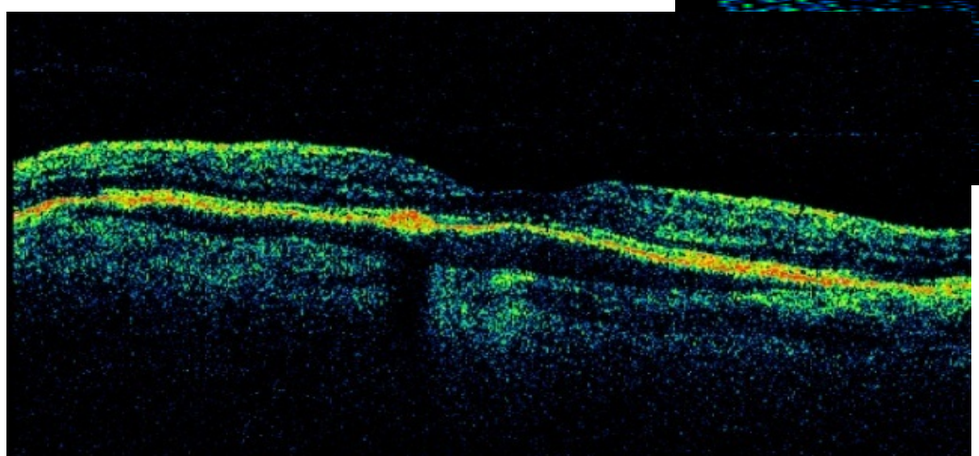
Lucentis 3x: GK: 0.5

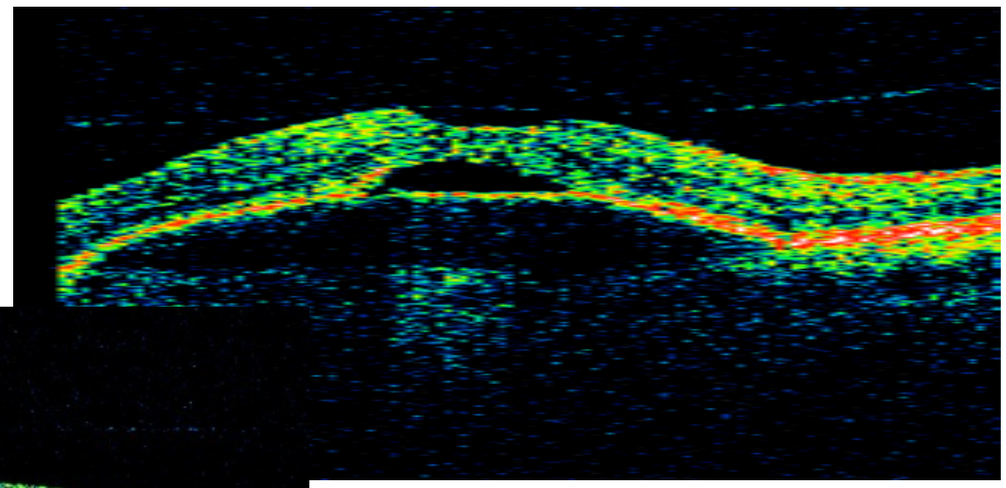


7.ay
GK: 0.7



1.ay



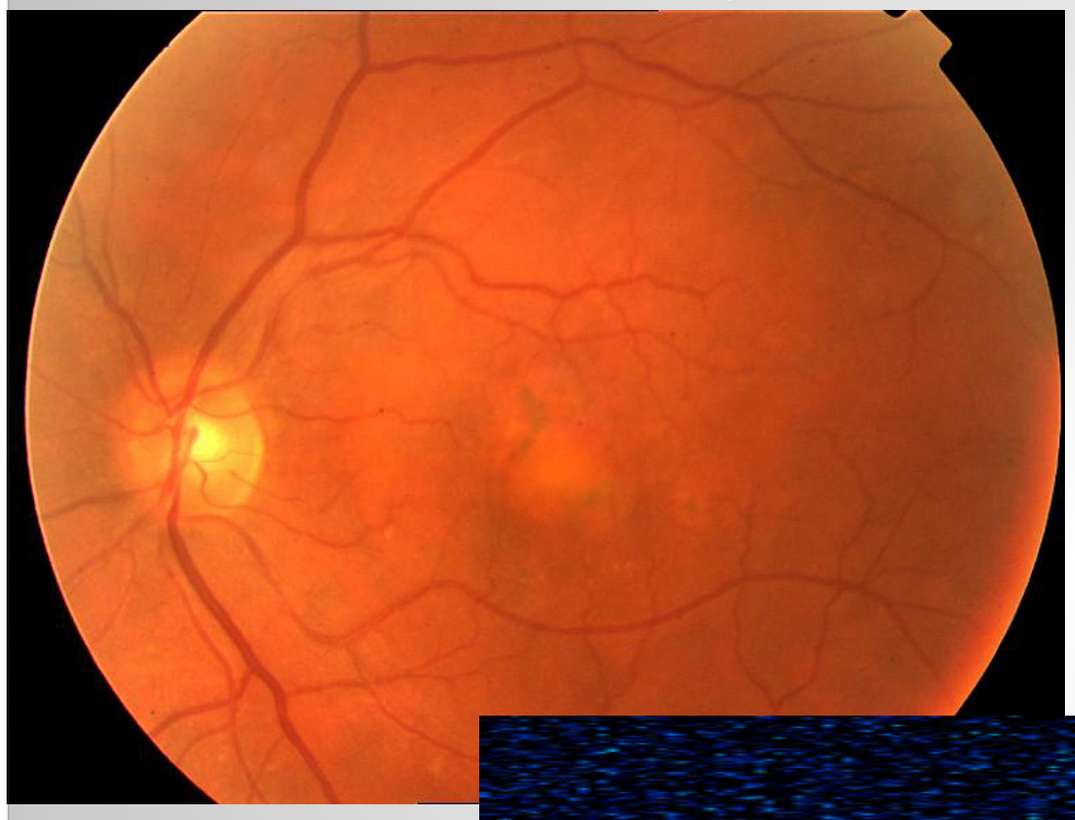


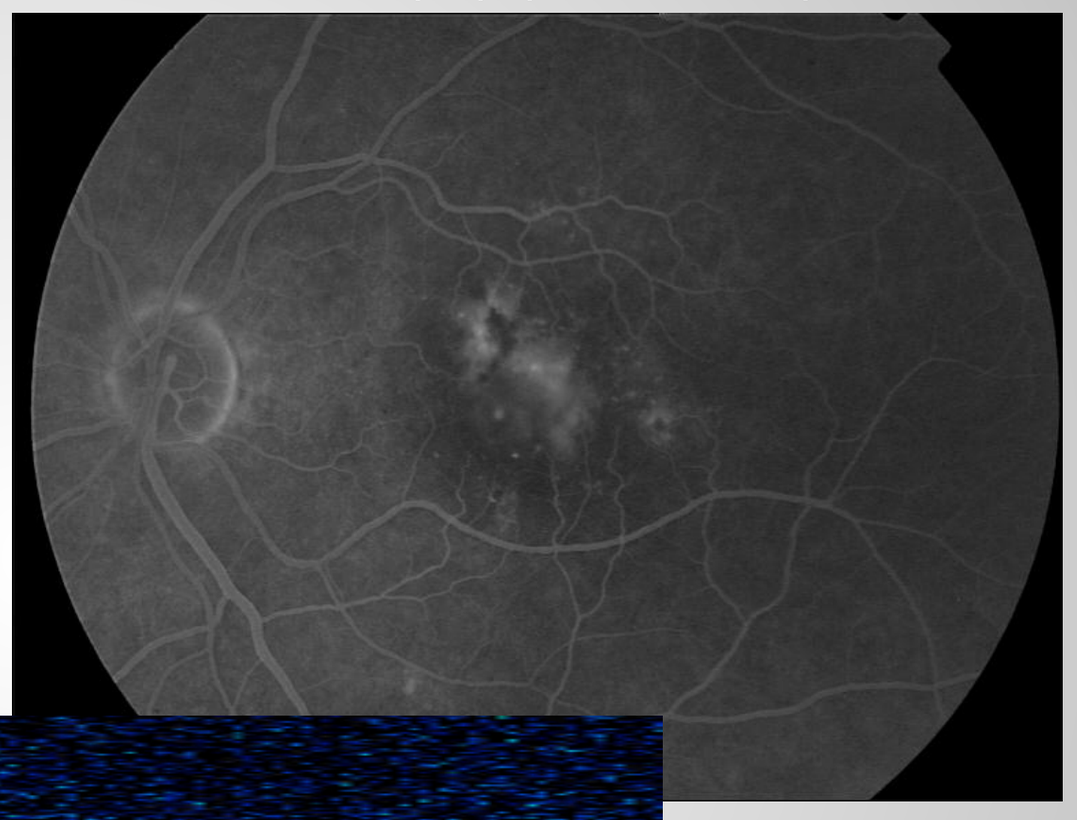
PDT

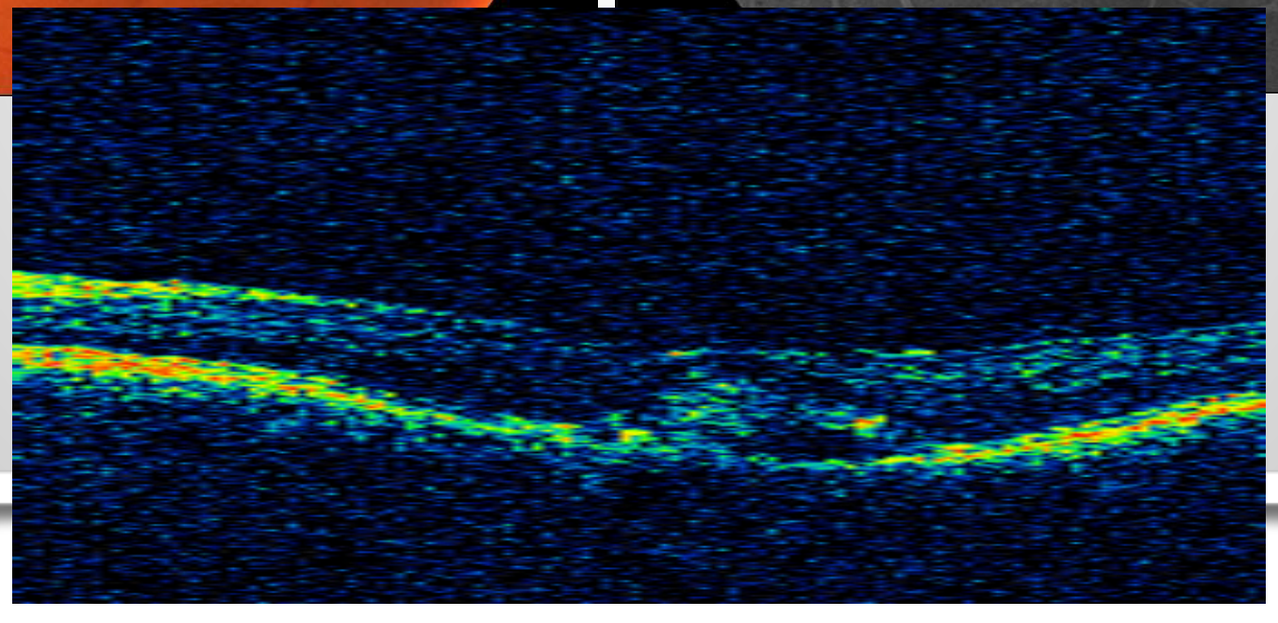
CEVAPSIZLIK

SWITCH

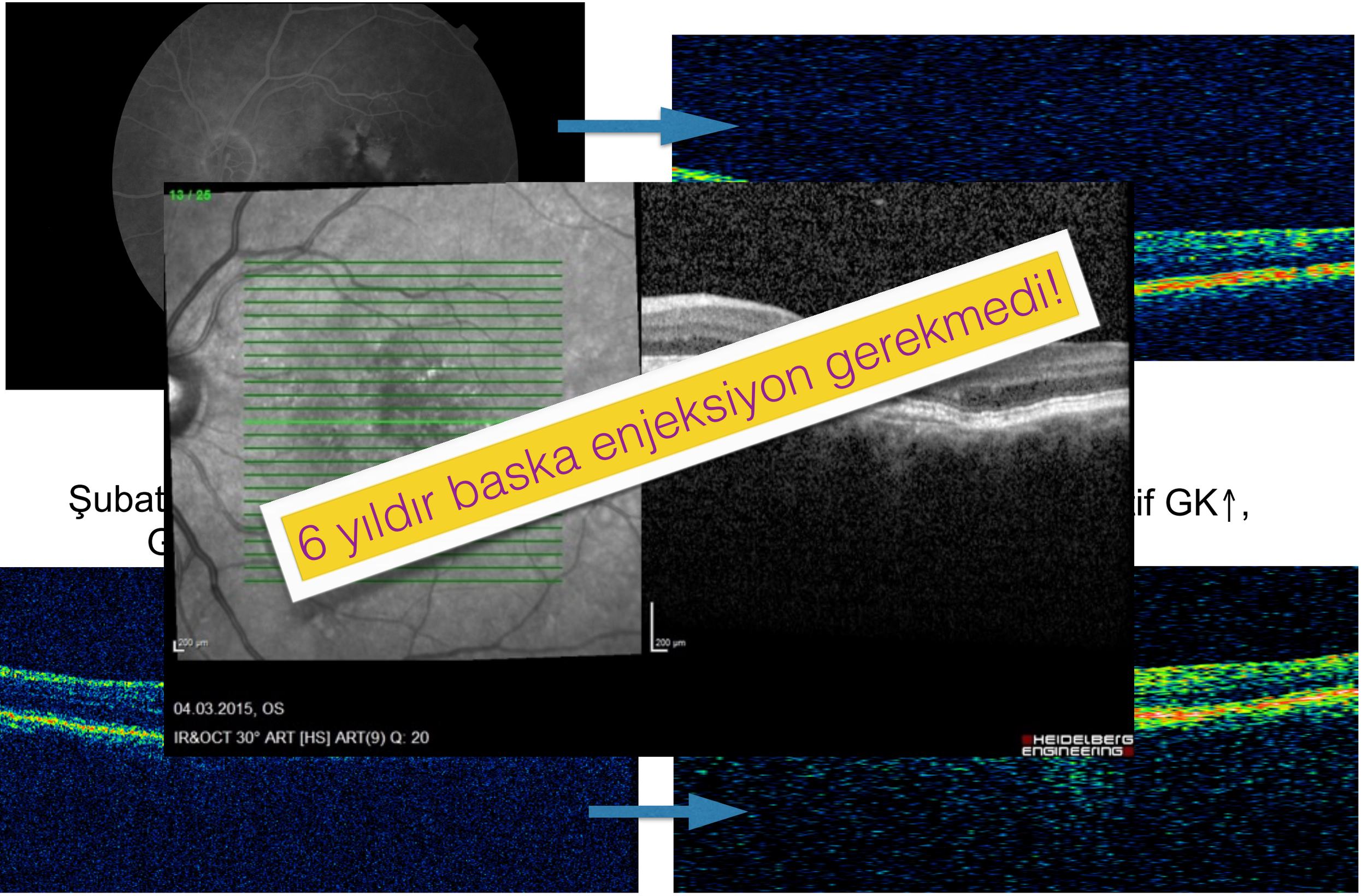
TA, Ressam, 64y, G: 0.7, AS: 7, IV Avastin (1.) (Kasım 09)







Ocak 2009, 2x Avastin, GK: 0.32, Subjektif GK↓, AS: 9
(1. Lucentis)



Şubat

if GK↑,
G

Anti-VEGF Tedaviye Cevapta Genetik Fakörler

- Türk toplumunda CFH (Y402H) ve VEGF rs2146323,rs699947 SNP'lerinin anti VEGF tedavi etkinliğine katkısı yoktur.*
- CFH genindeki rs1061170 polimorfizmi YBMD de anti-VEGF cevabının prediktörüdür. (homozigot mutantlarda tedaviye cevapta 1.6x azalma)**
- CFH, ARMS2, ve HTRA1 genleri ile tedavi cevabı arasında ilişki yok***

*Yıldız BK, Özdek Ş ve ark. EKSUDATİF YAŞA BAĞLI MAKULA DEJENERASYONUNDA ANTİ-VEGF TEDAVİ ETKİNLİĞİNİN GENETİK POLİMORFİZM İLE İLİŞKİSİ. TOD Ulusal Kongre, 2013

**Chen H, Yu KD, Xu GZ. Association between variant Y402H in age- related macular degeneration (AMD) susceptibility gene CFH and treatment response of AMD: a meta-analysis. PLoS One. 2012;7(8)

***Orlin A, et al. Association between high-risk disease loci and response to anti-vascular endothelial growth factor treatment for wet age related macular degeneration. Retina. 2012;32:4–9.

Cevapsızlık
VMT-ERM Varlığı

EPIRETINAL MEMBRANES IN NEOVASCULAR AGE-RELATED MACULAR DEGENERATION

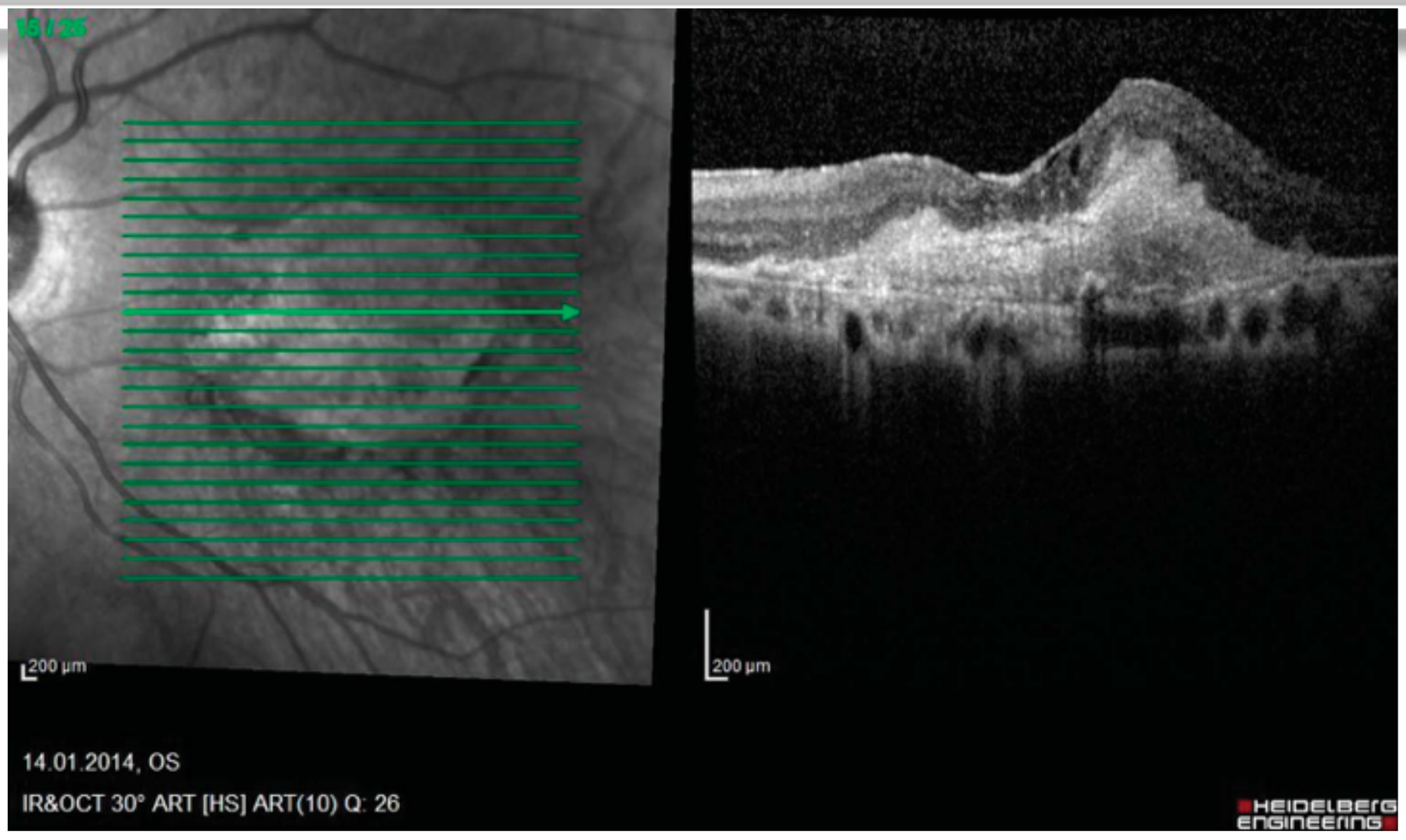
Effect on Outcomes of Anti-vascular Endothelial Growth Factor Therapy

EMINE ESRA KARACA, MD,*‡ BURÇIN KEPEZ YILDIZ, MD,†‡ MEHMET ÖZGÜR ÇUBUK, MD,‡ ŞENGÜL ÖZDEK, MD‡

Purpose: To investigate the role of epiretinal membrane (ERM) on outcomes of anti-vascular endothelial growth factor therapy in patients with neovascular age-related macular degeneration (nAMD).

- Karaca EE, Kepez YB, Çubuk MÖ, Özdek Ş. Epiretinal membranes in neovascular age-related macular degeneration: effect on outcomes of anti-VEGF therapy. **Retina. 2015**

Cevapsızlık
VMT-ERM Varlığı



- Karaca EE, Kepez YB, Çubuk MÖ, Özdek Ş. Epiretinal membranes in neovascular age-related macular degeneration: effect on outcomes of anti-VEGF therapy. Retina. 2015

Cevapsızlık
VMT-ERM Varlığı

Table 1. Baseline Characteristics of the Patients in Three Groups

	Group 1 (n = 43)	Group 2 (n = 29)	Group 3 (n = 18)	*P* (ANOVA)
Age (years)	70.5 ± 1.3	70.3 ± 1.3	69.11 ± 1.3	0.919
Sex (M/F)	18/25	11/18	6/12	0.274
CNV type (occult/classical)	34/9	20/9	13/5	0.651
Follow-up time (month)	31.5 ± 3.2	25.1 ± 2.5	29.72 ± 0.4	0.274
BCVA (baseline) (logMAR)	0.5 (0.1–1)	0.5 (0.1–1)	0.3 (0–1)	0.204
CFT (μm) (baseline)	252 (140–651)	271 (126–1,000)	255 (175–600)	0.525
Lesion size (cm^2) (baseline)	9.97 (0.21–71.37)	10.23 (0.65–33.12)	11.29 (1.38–37.31)	0.230
No. injections	8.32 ± 4.7	6.87 ± 3.3	11.6 ± 2.9	**<0.001**
Injection intervals (weeks)	7.59 (4–10.7)	7.2 (4–12.2)	6.12 (4–9.1)	**<0.032**
Longest interval between injections (weeks)	10.7	12.2	9.1	**<0.012**

ANOVA, analysis of variance; CFT, central foveal thickness; CNV, choroidal neovascularization.

- Karaca EE, Kepez YB, Çubuk MÖ, Özdek Ş. Epiretinal membranes in neovascular age-related macular degeneration: effect on outcomes of anti-VEGF therapy. Retina. 2015

ANTİ-VEGF TEDAVİDE DİRENÇ

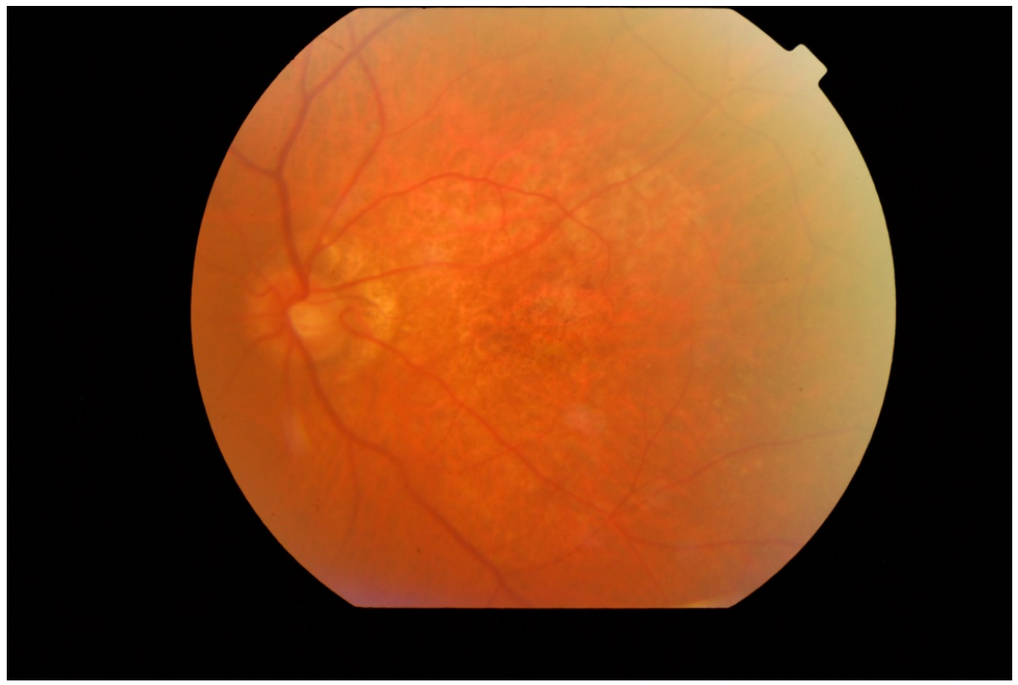
- YANLIŞ TANI (%46.2)

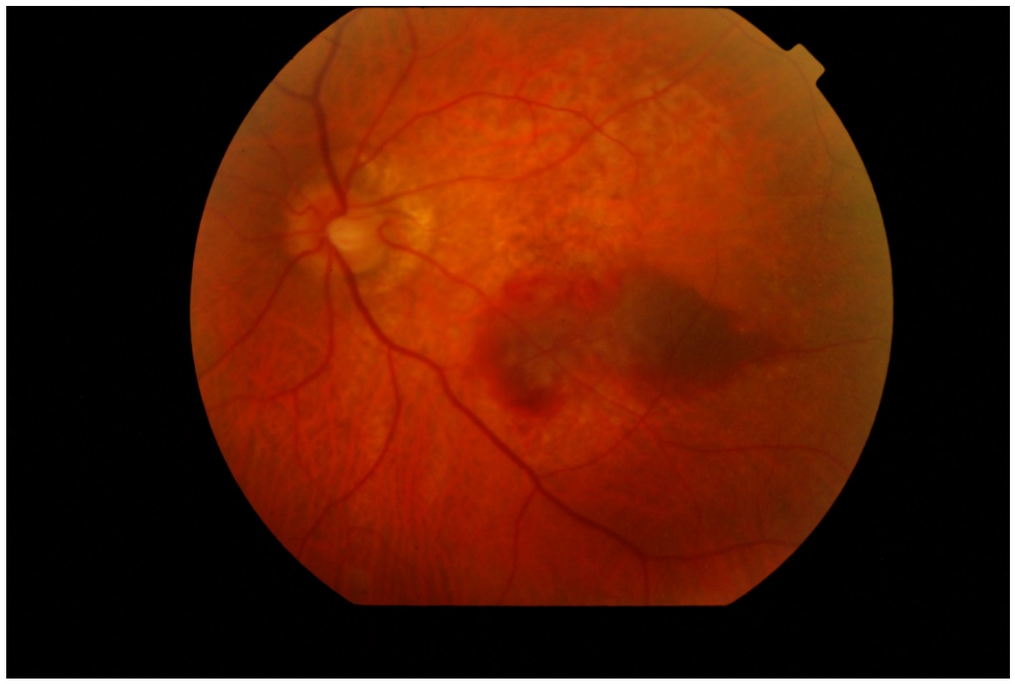
  -PCV, RAP, VİTELLİFORM, SSKR

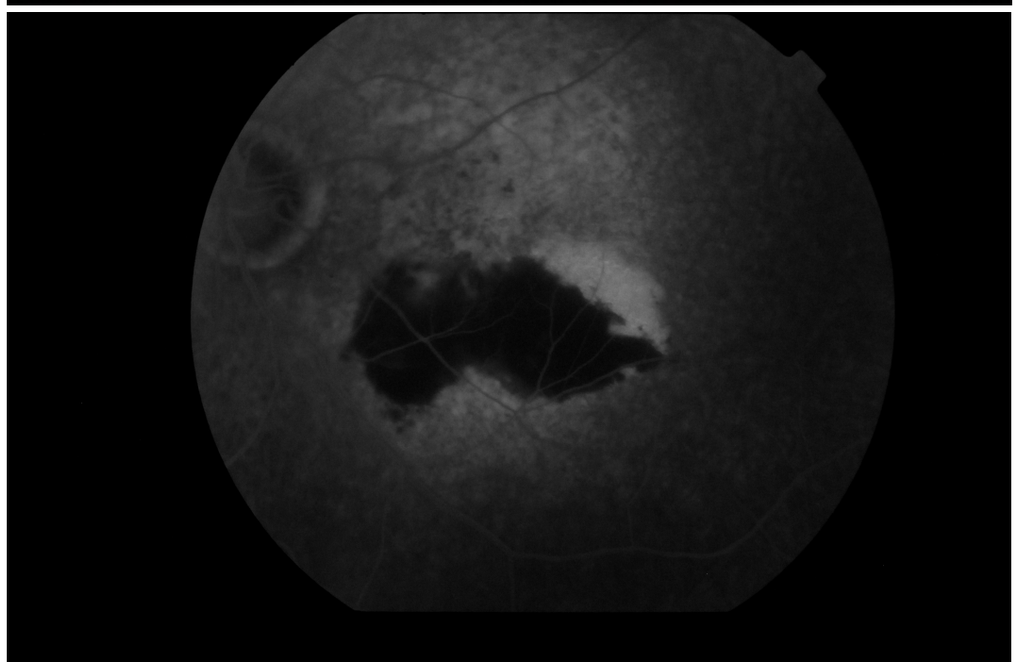
- TAŞİFLAKSİ-TOLERANS (%22)
- CEVAPSIZLAR (%26.9) (İLK 3 DOZ İLE SIVI↑ VEYA GK↓)
- HEMORAJİK CEVAP
- KOMPLİKASYONLAR: RPE yırtığı, atrofi, skar oluşumuna bağlı görme kaybı (%11.6)

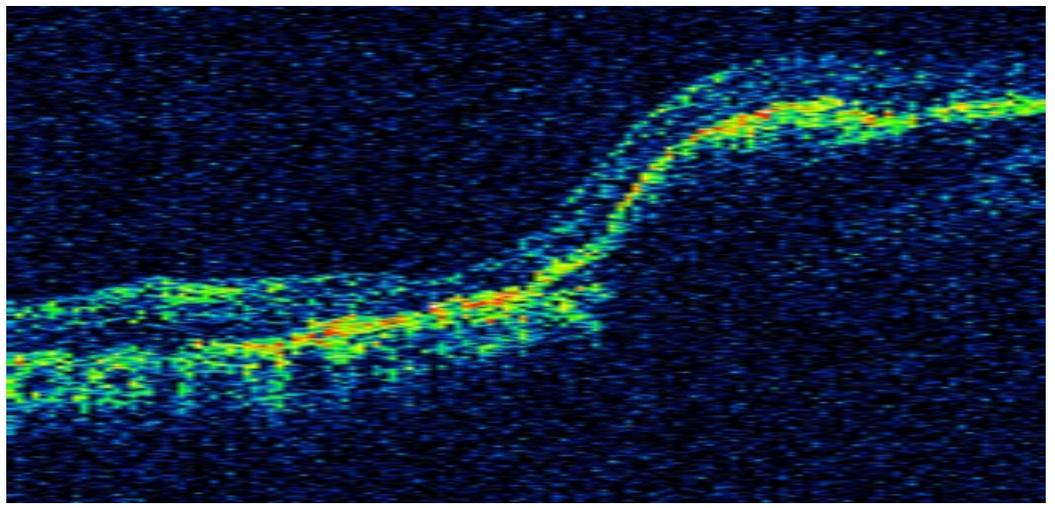
HEMORAJİK CEVAP

72y, Ocak 09, GK: 0.1, PED, IV Lucentis, AS:11



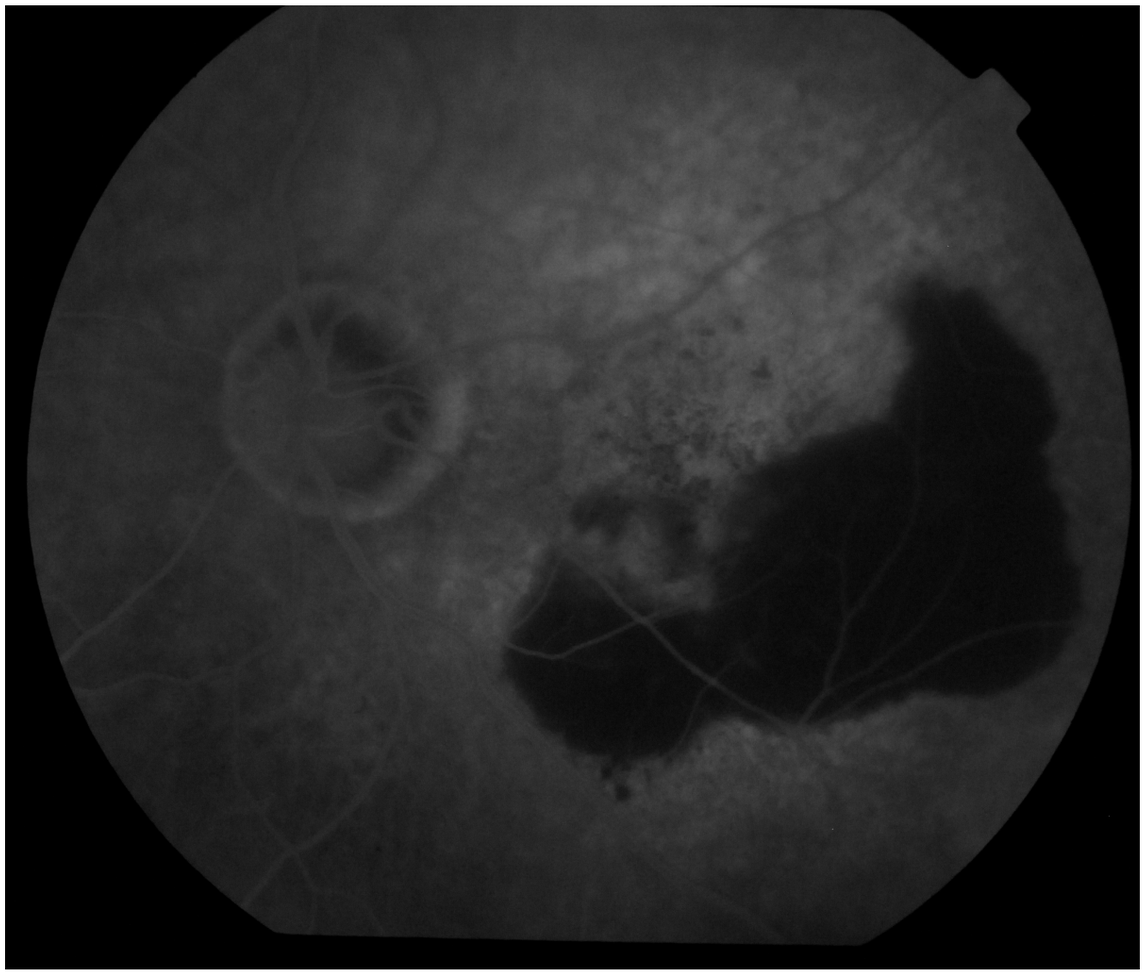


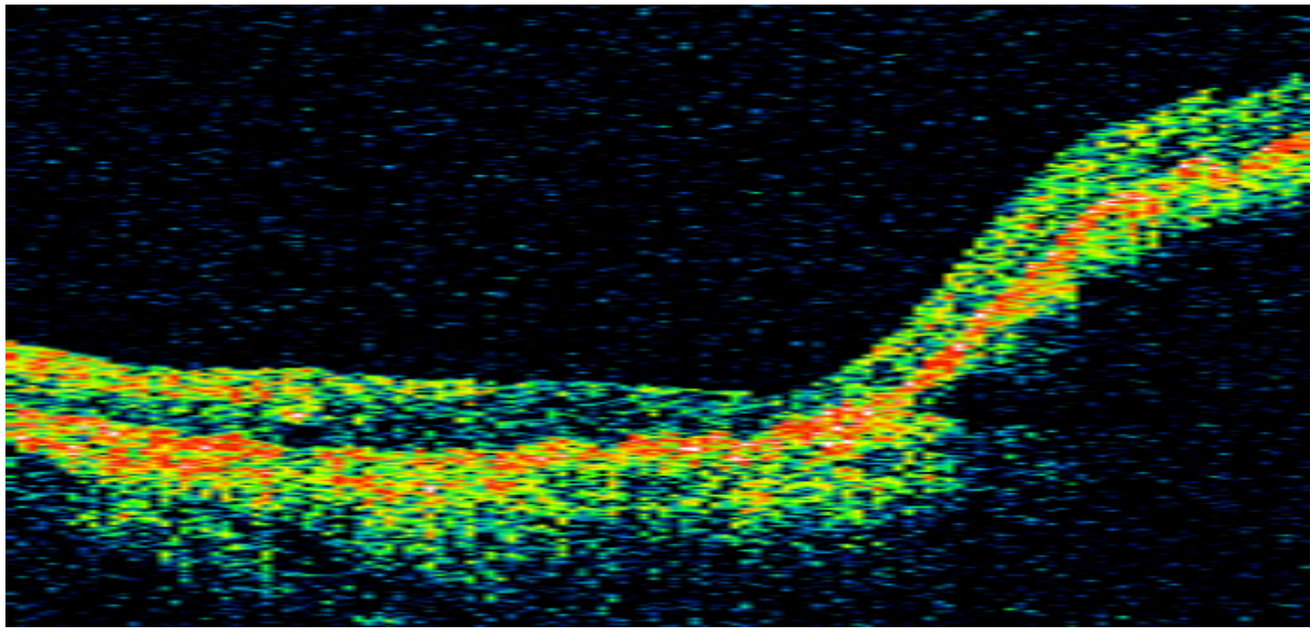




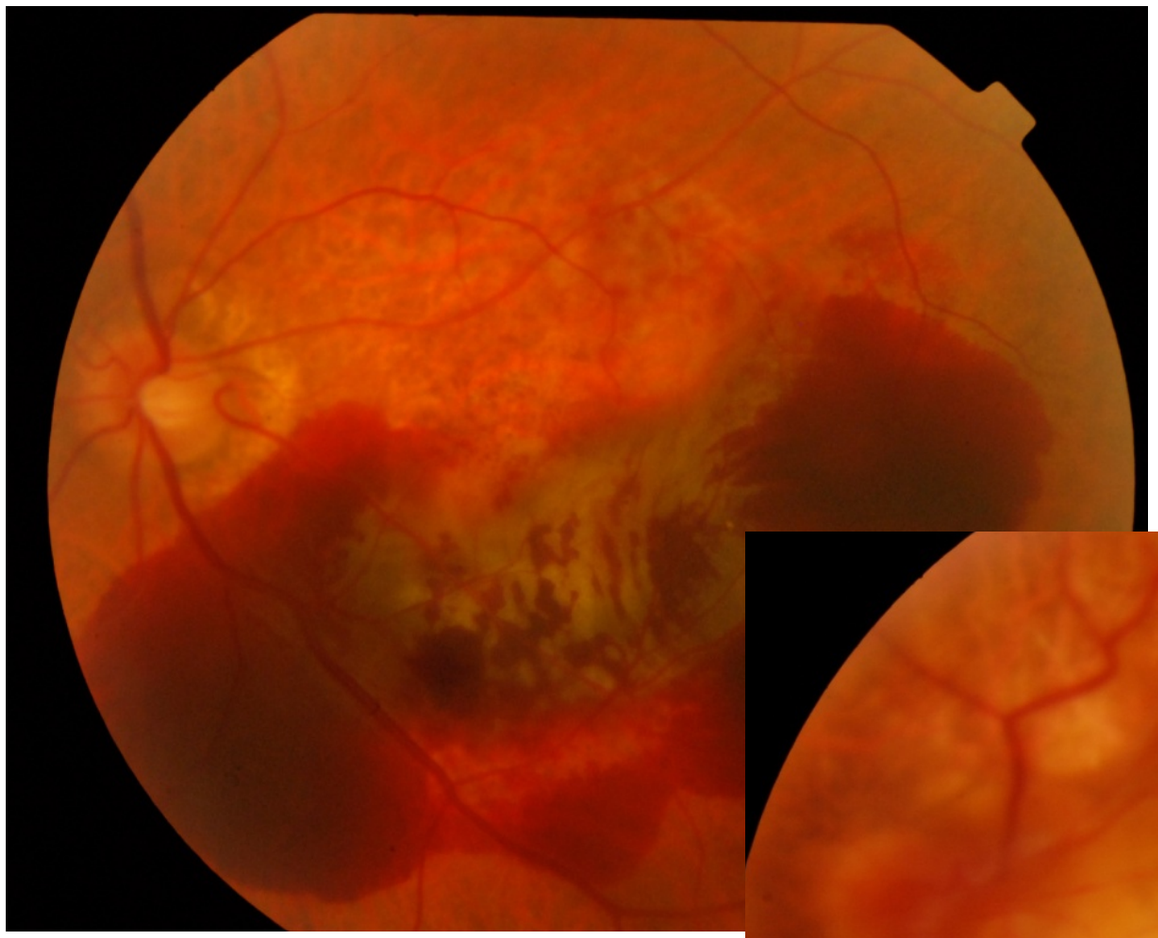
Şubat 09, GK: 4mps, 2. Lucentis, AS: 13

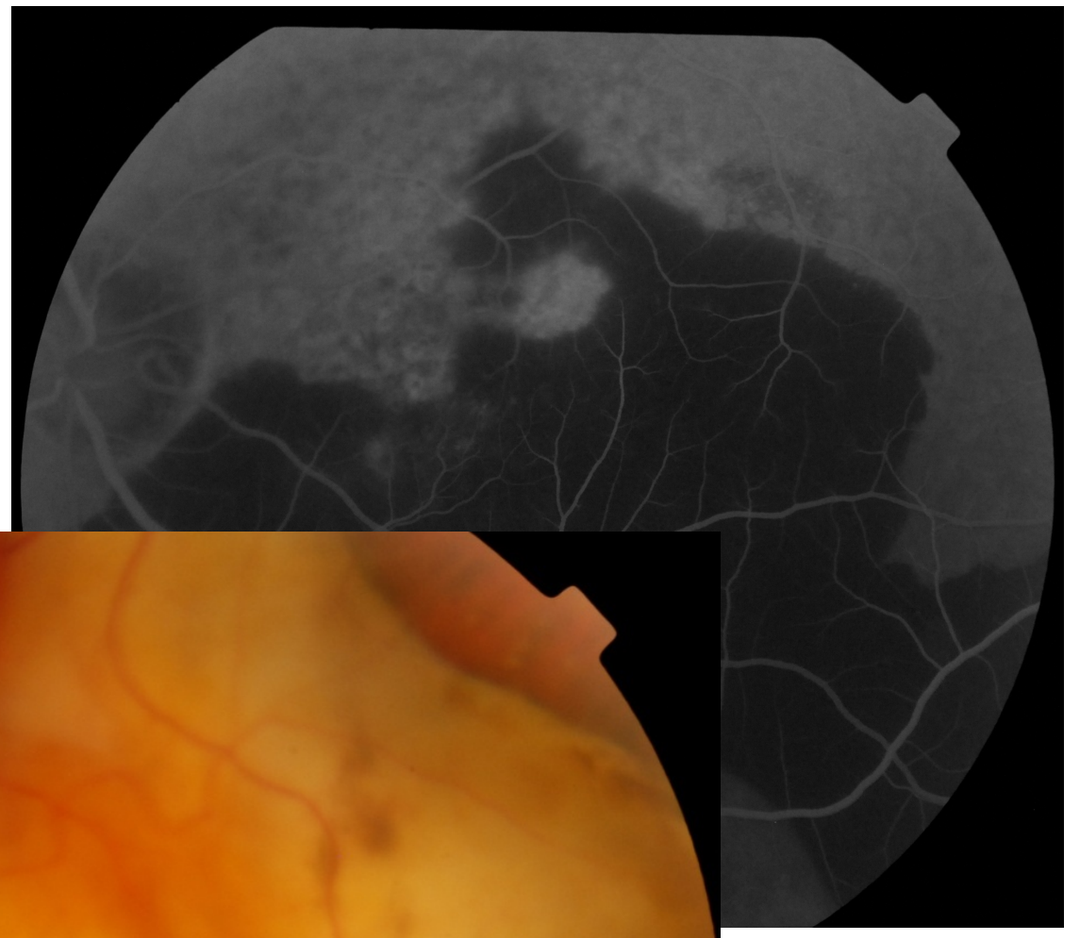


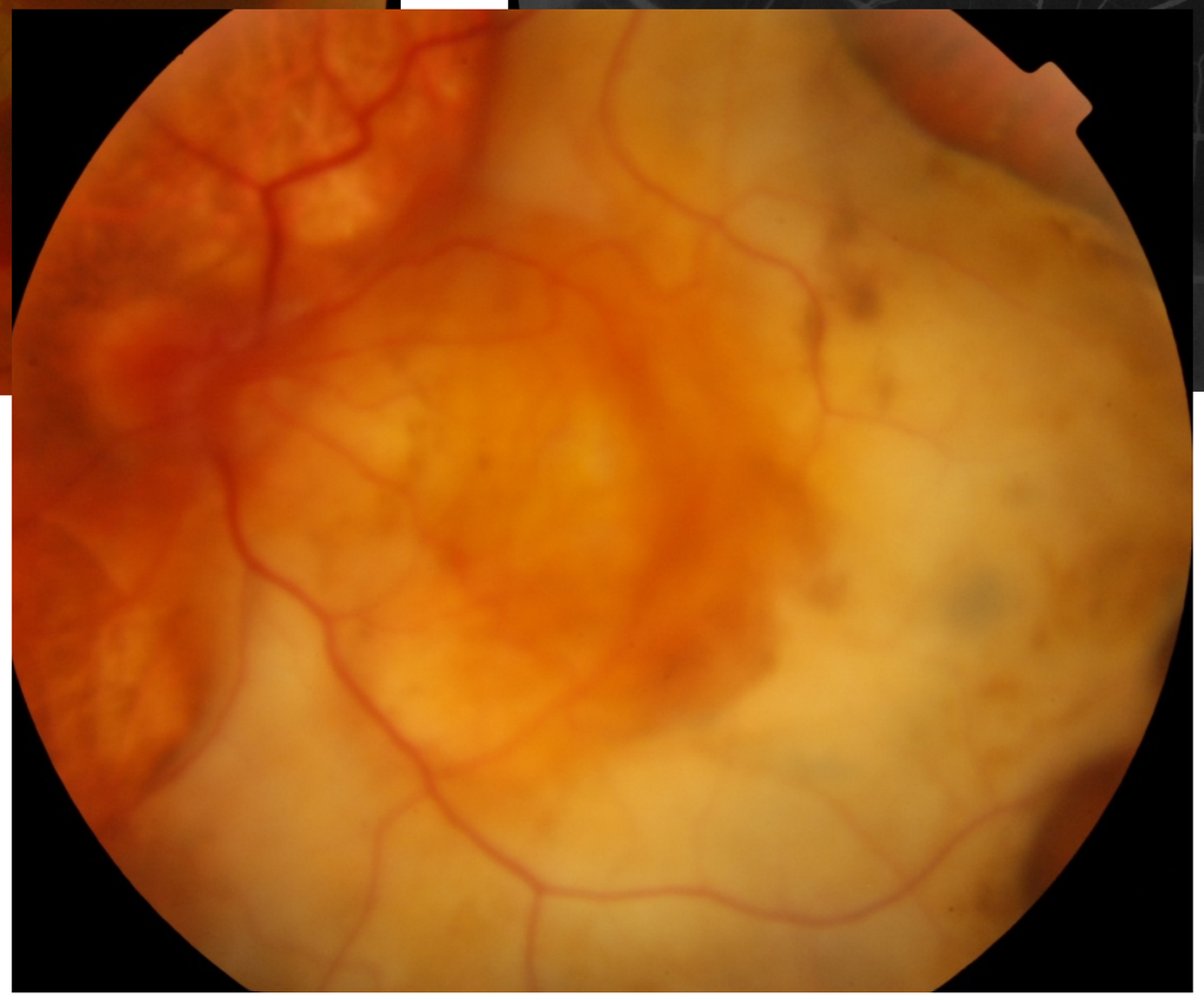




Mart 09, GK: 3mps, AS: 13

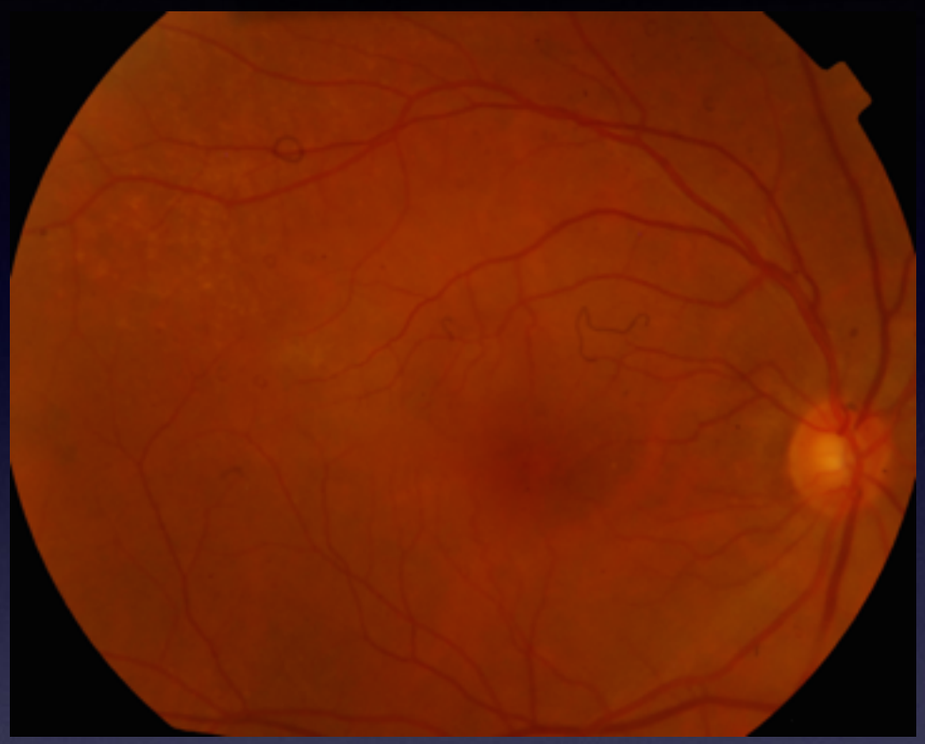




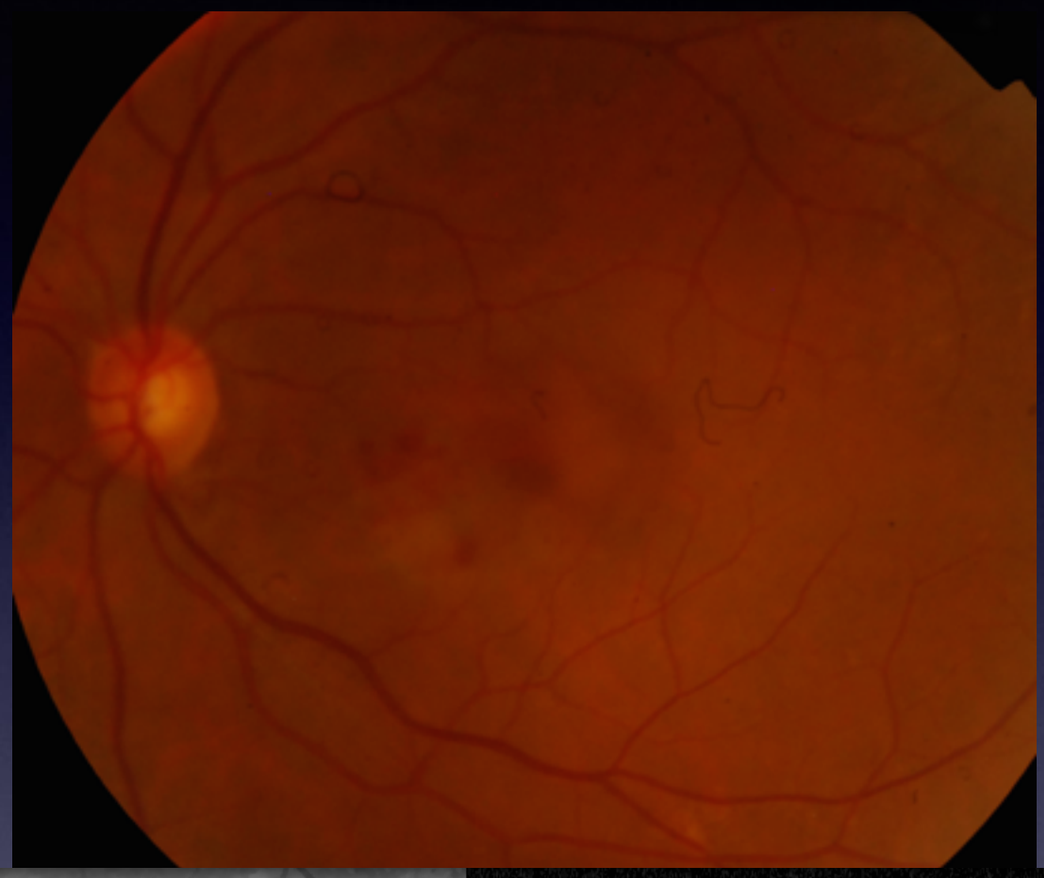


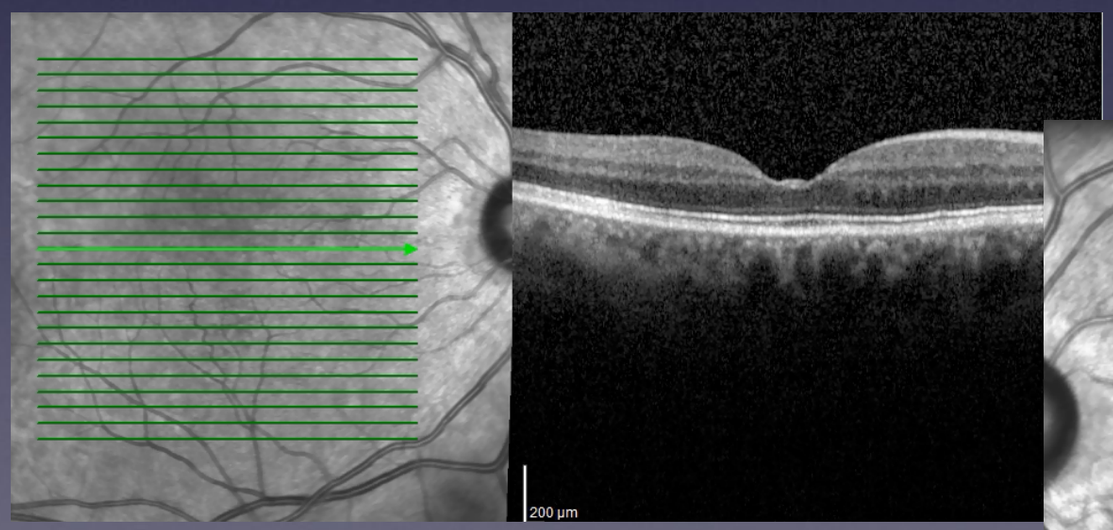
HEMORAJİK CEVAP

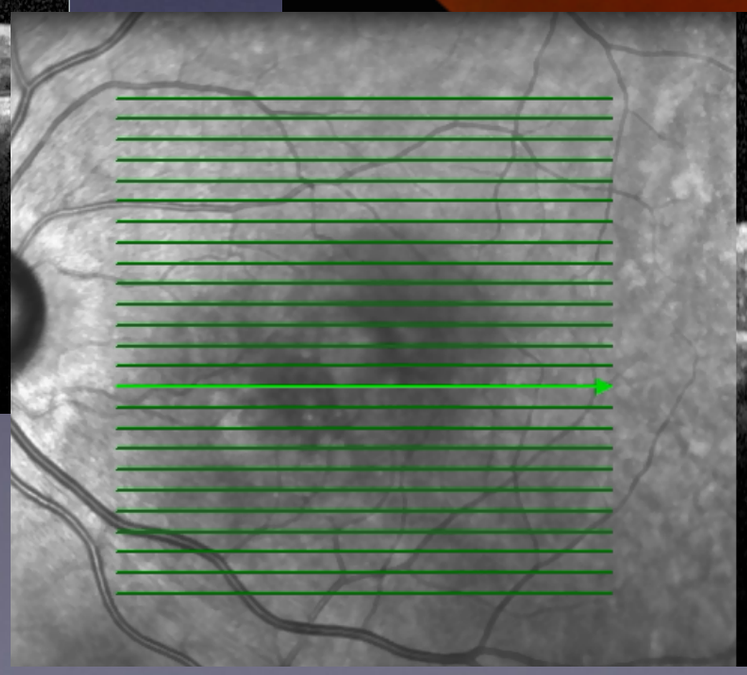
SG, 63y, GK: 0.6, Tip 1 KNV

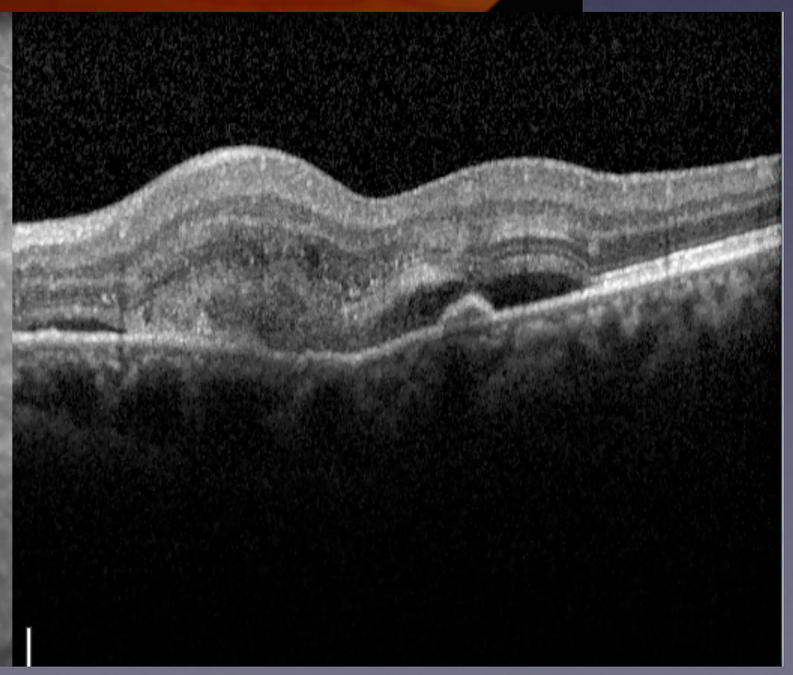


11/2013







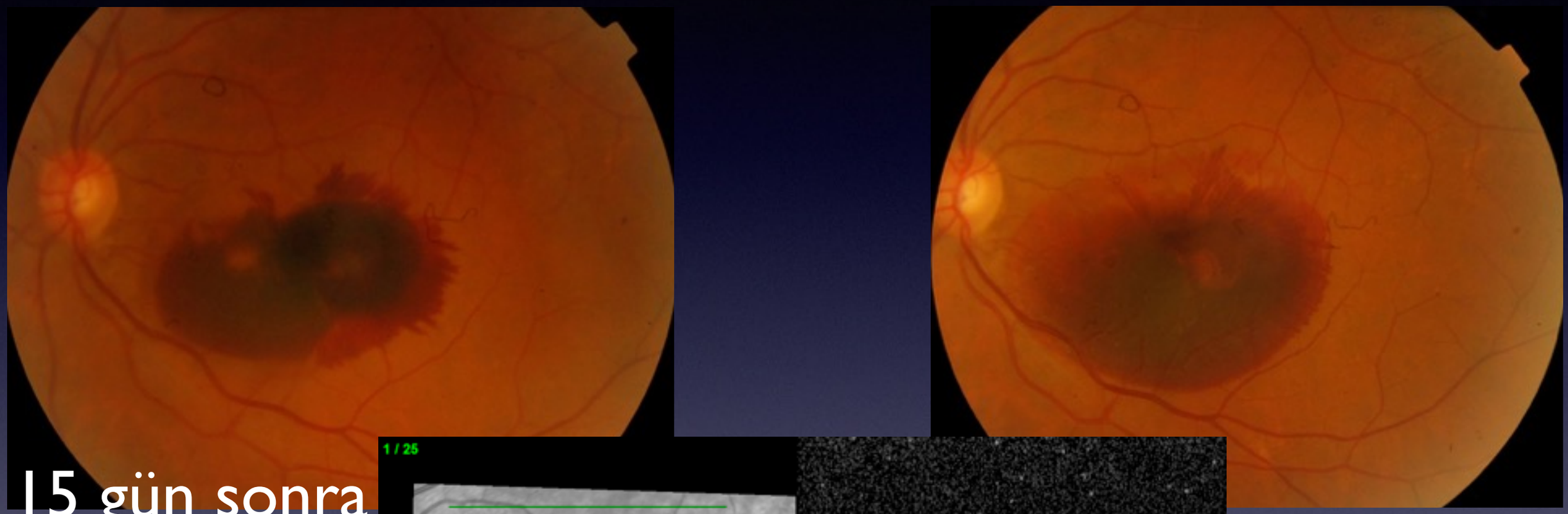




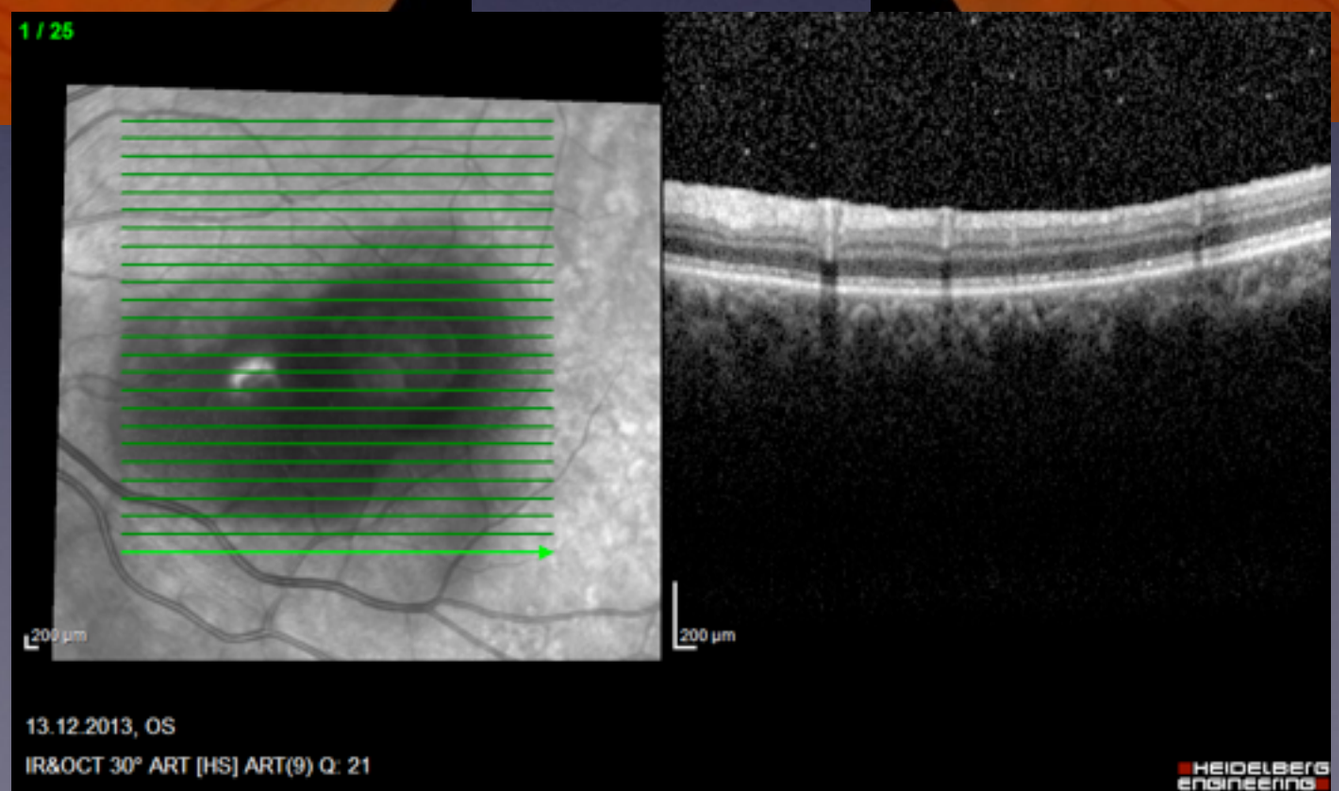
IV Lucentis

HEMORAJİK CEVAP

IV Lucentis+tPA+SF6+Yüzüstü pozisyon



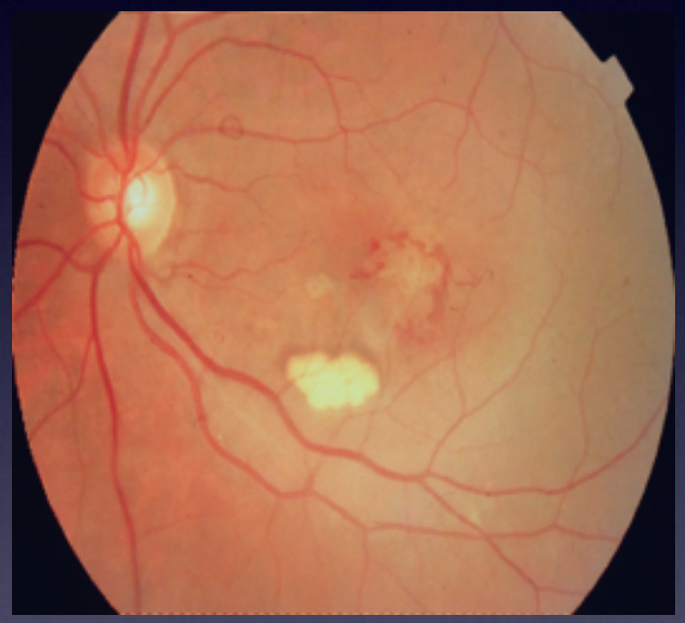
15 gün sonra



1. ay:
GK: 0.4
Lucentis

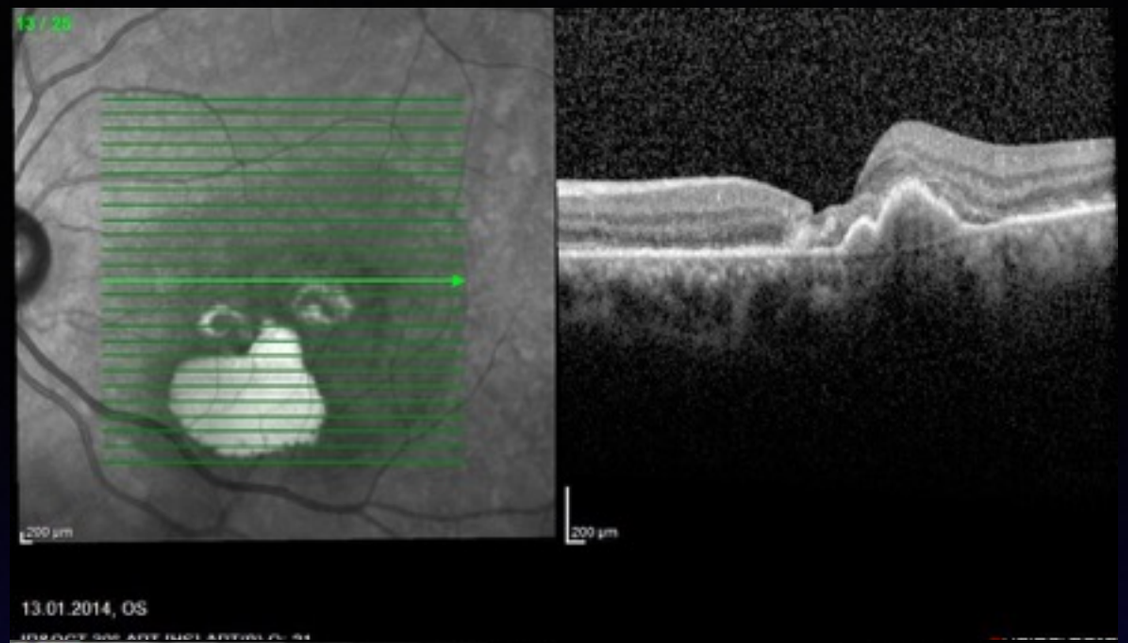


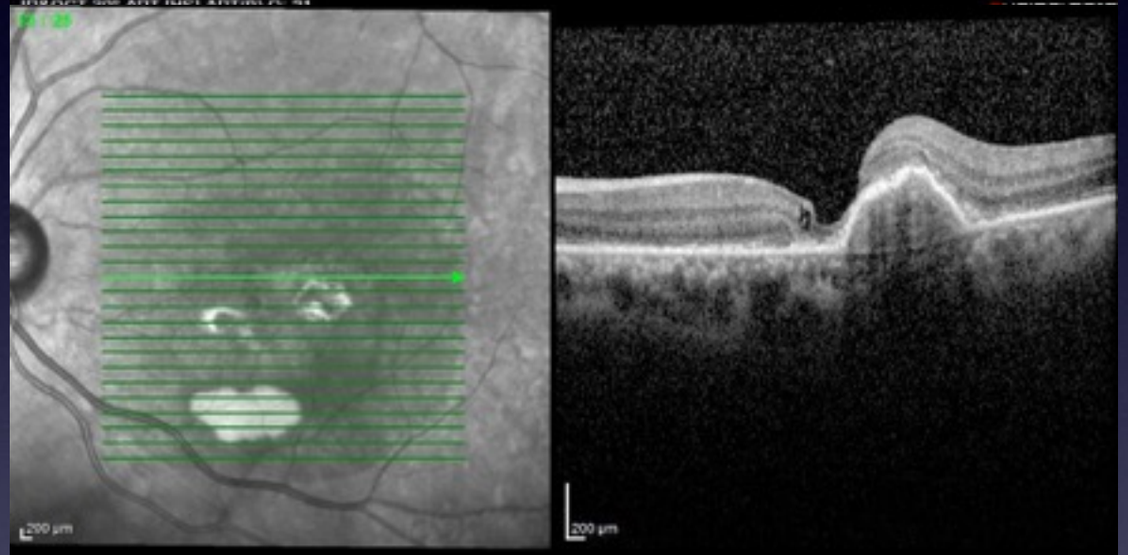
2. ay:
GK: 0.6
Lucentis

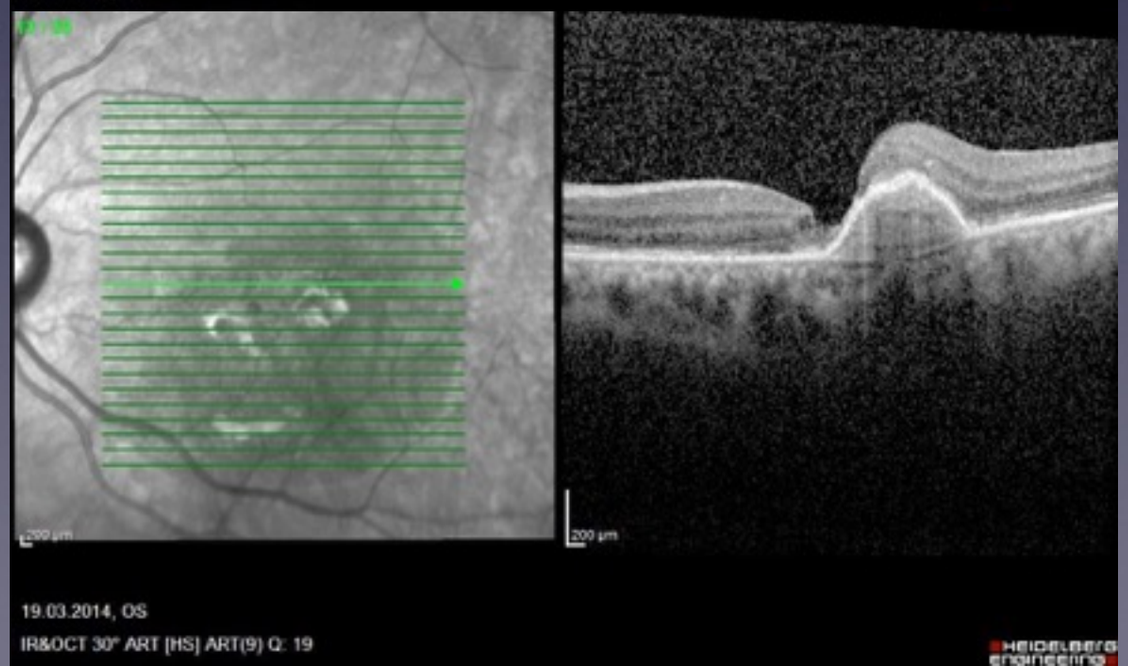


4x Lucentis
GK: 0.7





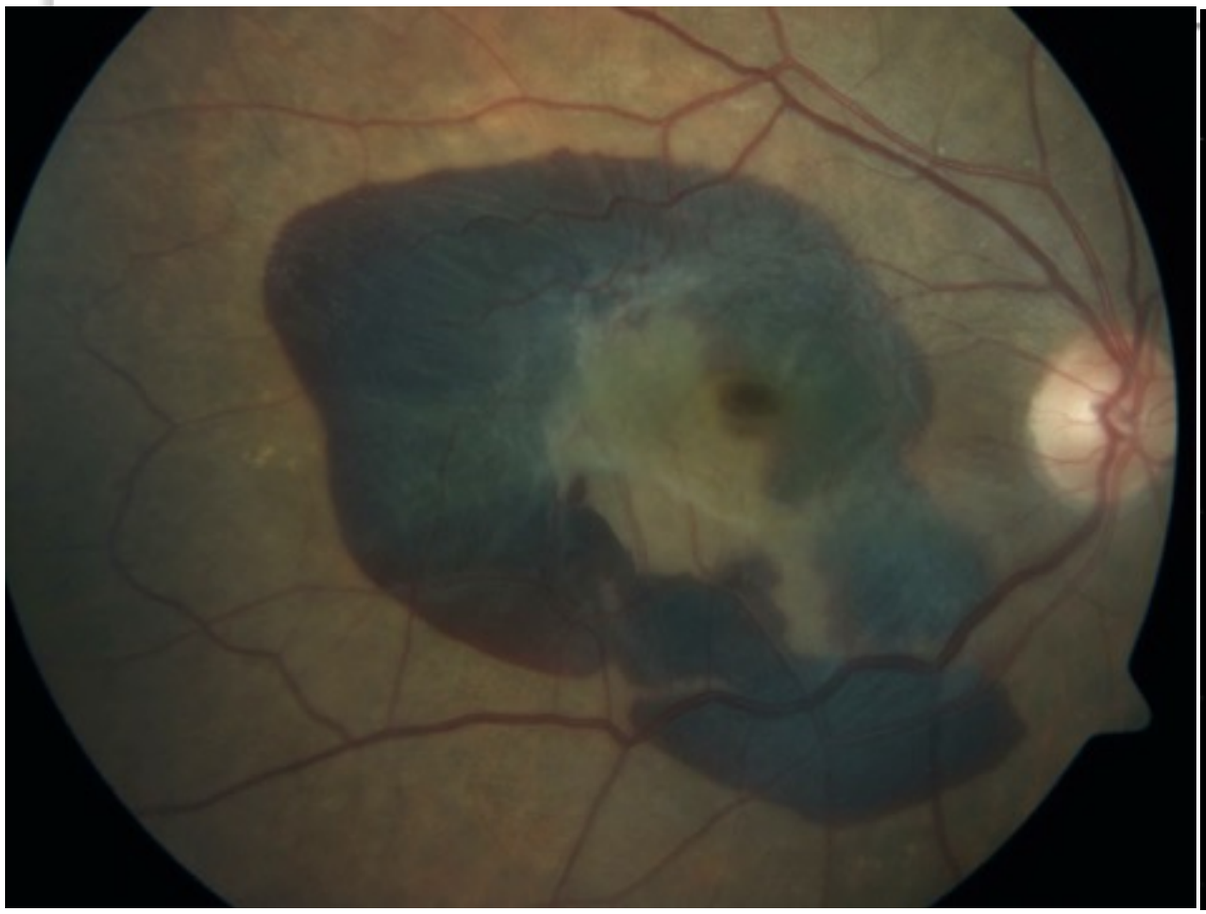




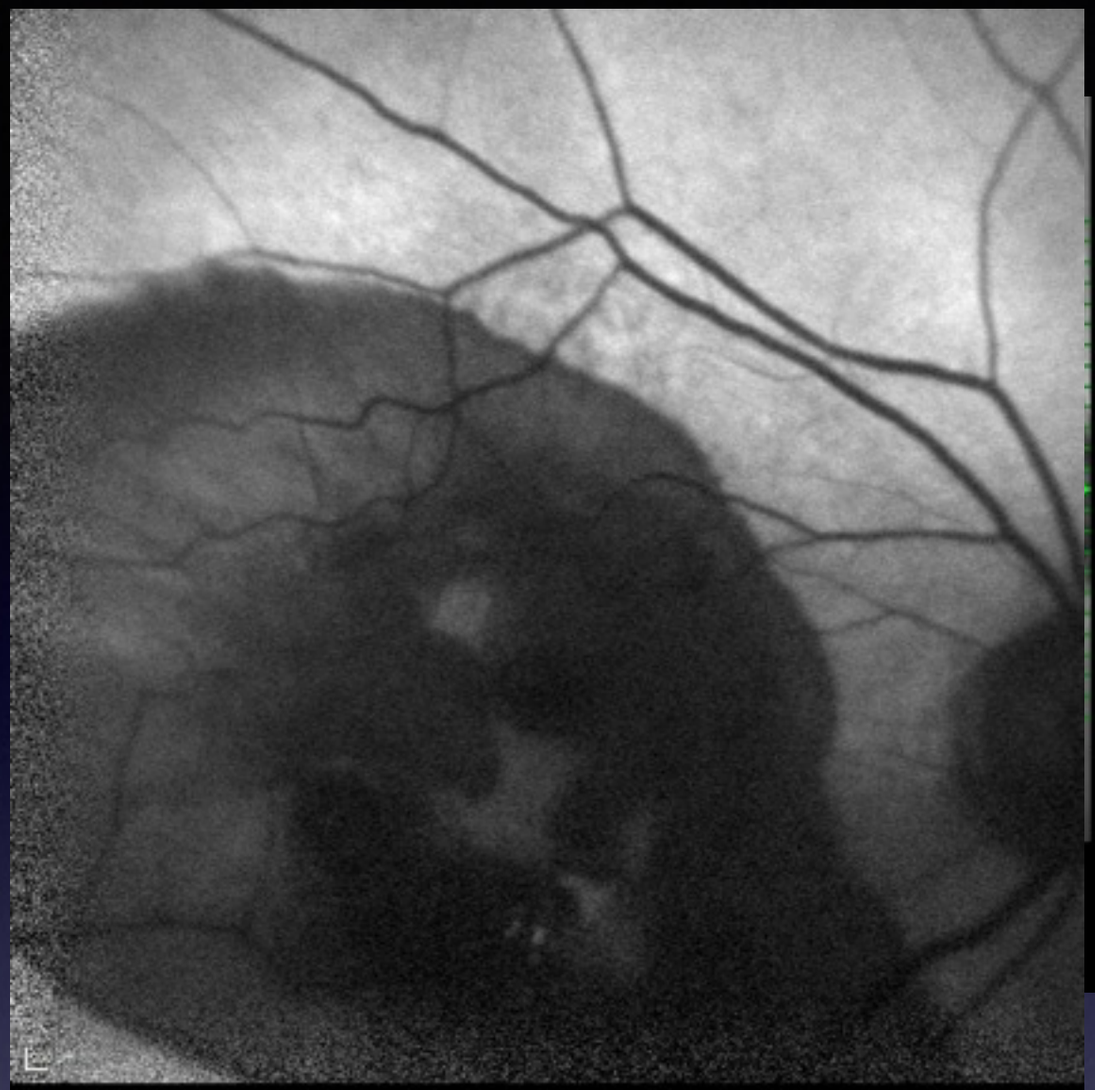
HEMORAJİK CEVAP

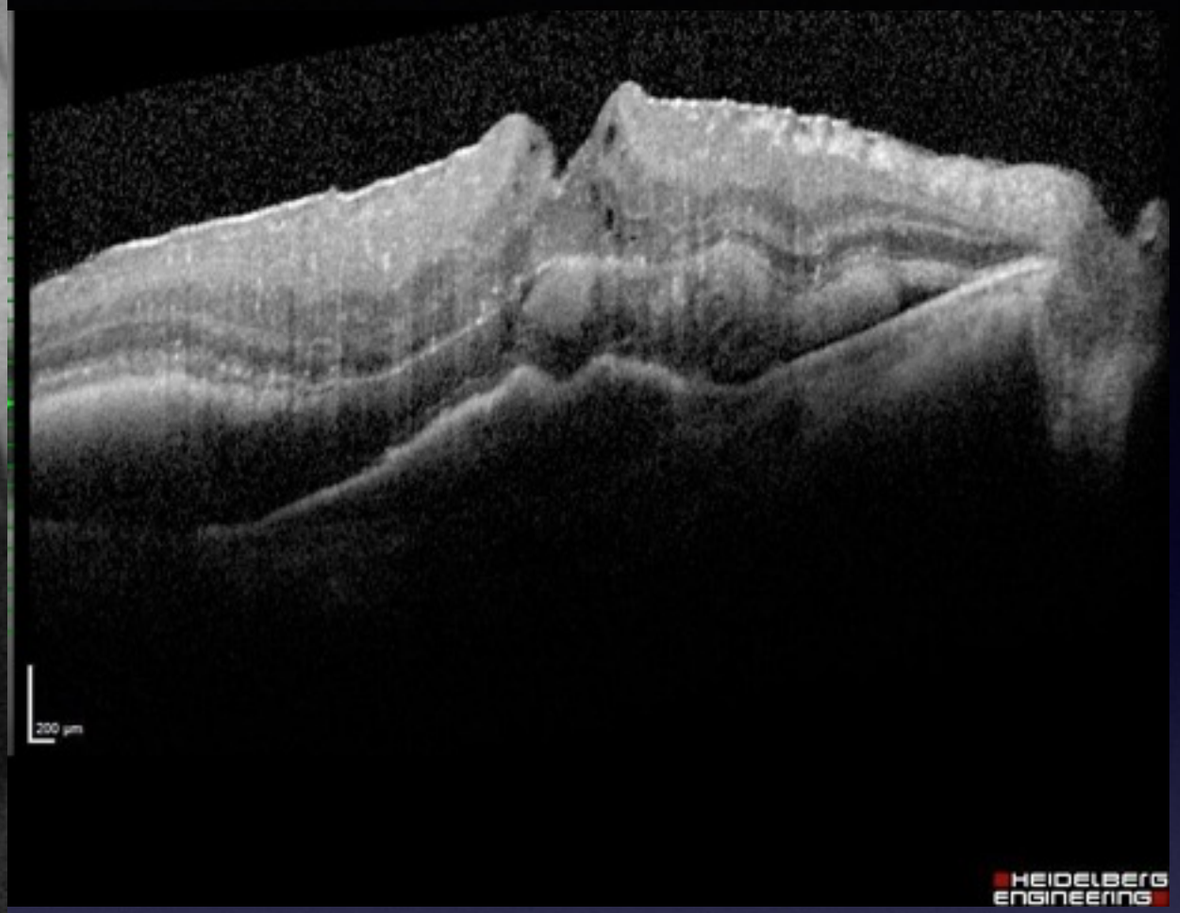
NT, 65y, F, GK: Imps

ERM, Makuler Hol

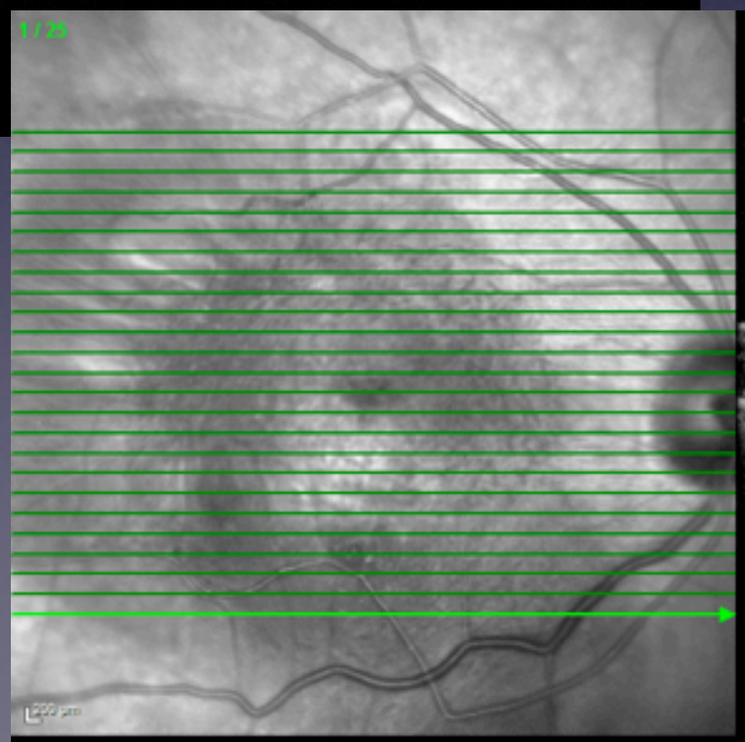


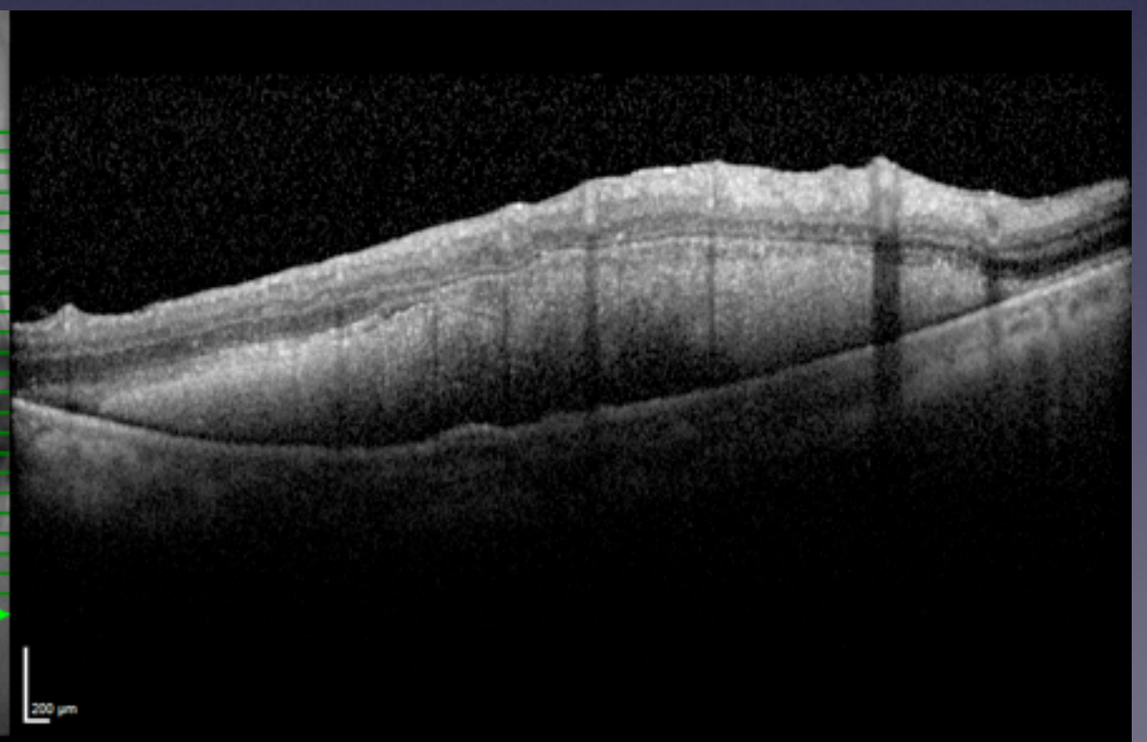






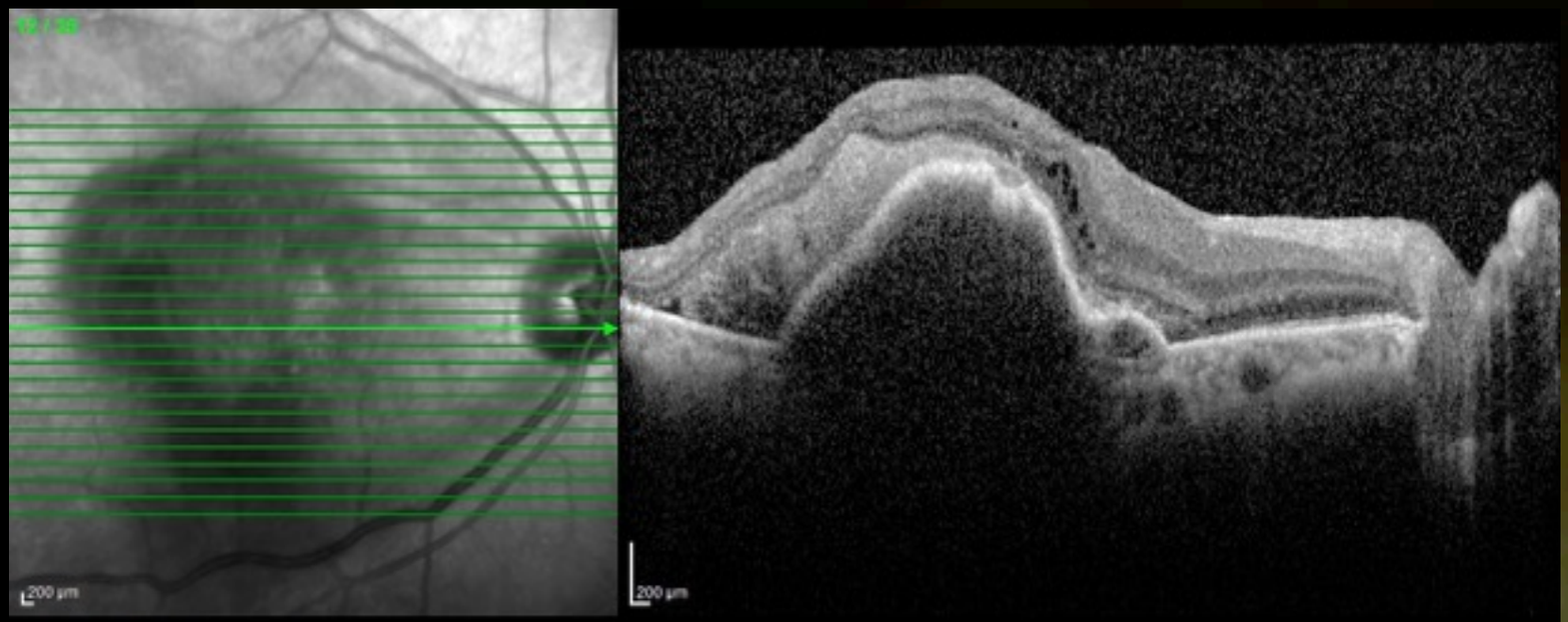
17.3.2014, OD
BAF 30° ART(50)



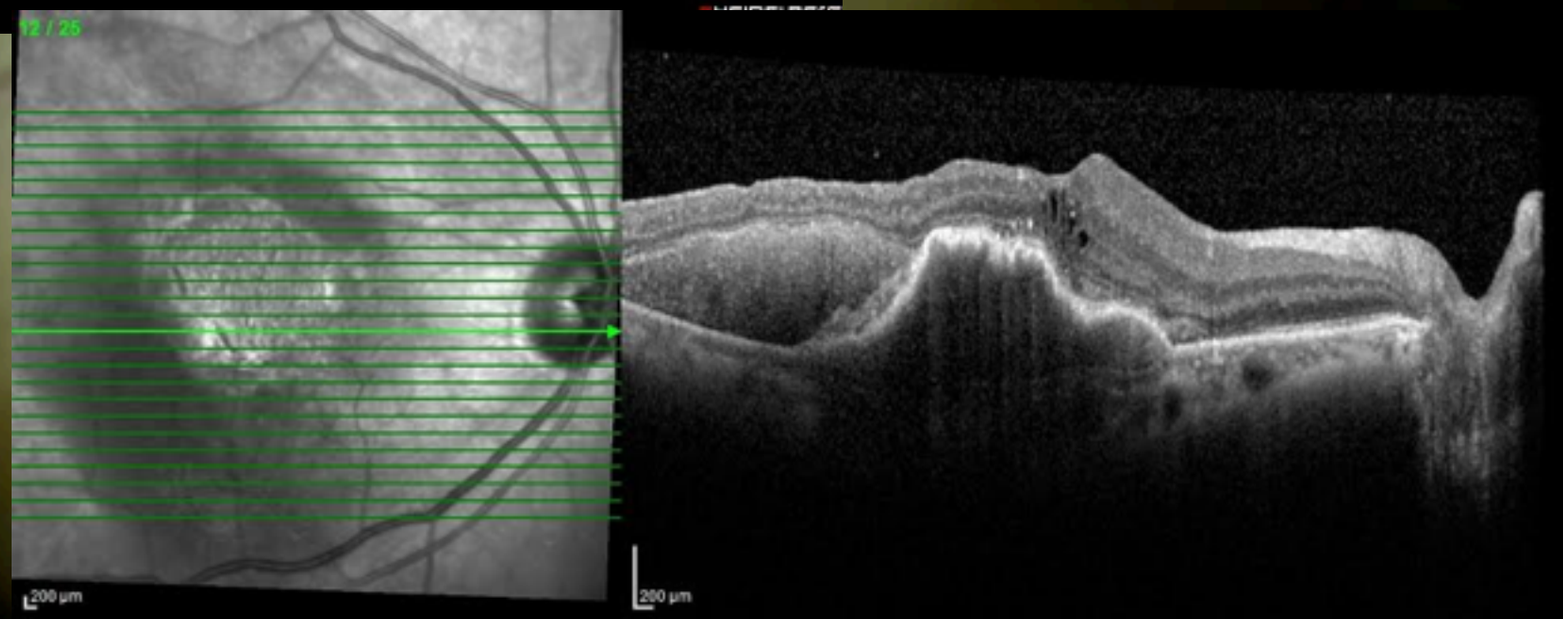


17.3.2014, OD

Cerrahi: PPV-MP-ILMP-Subretinal tPA-Gaz



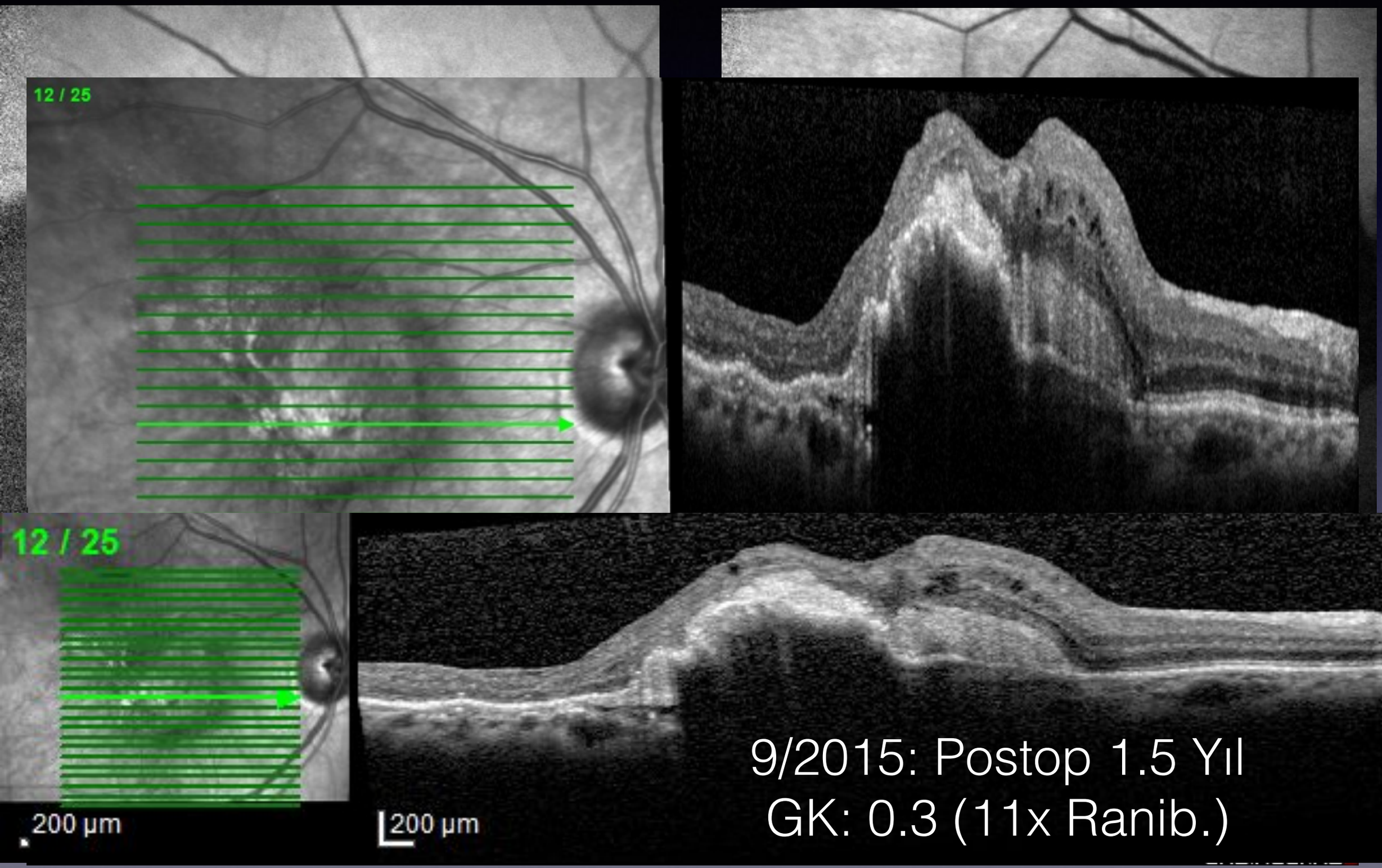
TASBAS, NIGAR, 01.01.1939
28.03.2014, OD
IR&OCT 30° [HS] ART(9) Q: 23



TASBAS, NIGAR, 01.01.1939
15.04.2014, OD
IR&OCT 30° [HS] ART(9) Q: 28

HEIDELBERG ENGINEERING

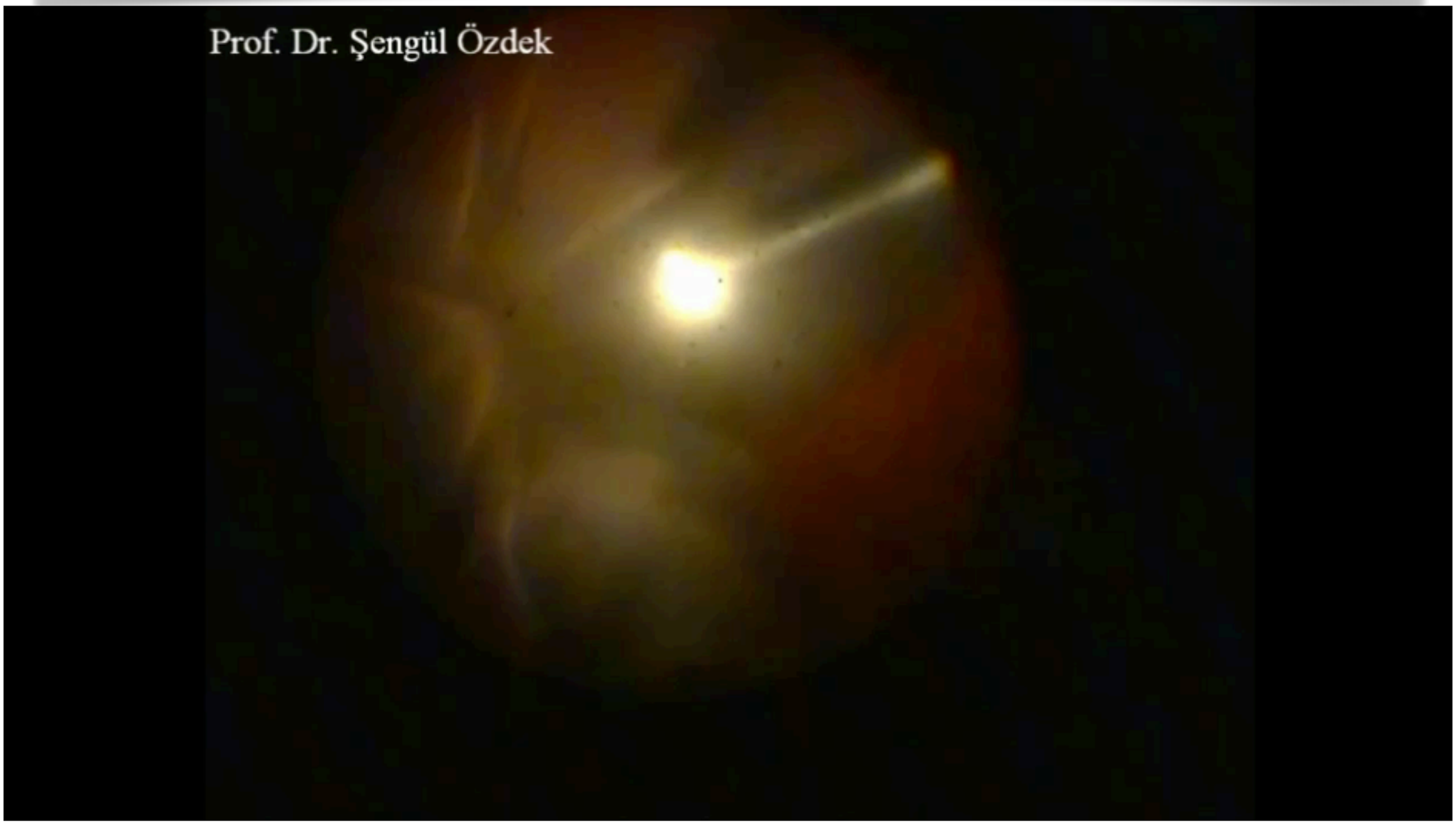
Postop 1.ay, GK: 0.2, Ranibizumab'a devam



HEMORAJİK CEVAP

68, GK: zayıf EH,

2 gün önce ani görme kaybı (anti-VEGF almaktayken)



ANTİ-VEGF TEDAVİDE DİRENÇ

- YANLIŞ TANI (%46.2)

  -PCV, RAP, VİTELLİFORM, SSKR

- TAŞİFLAKSİ-TOLERANS (%22)

- CEVAPSIZLAR (%26.9) (İLK 3 DOZ İLE SIVI↑ VEYA GK↓ **AS!**)

- HEMORAJİK CEVAP

- KOMPLİKASYONLAR: RPE yırtığı, atrofi, skar oluşumuna bağlı görme kaybı (%11.6)

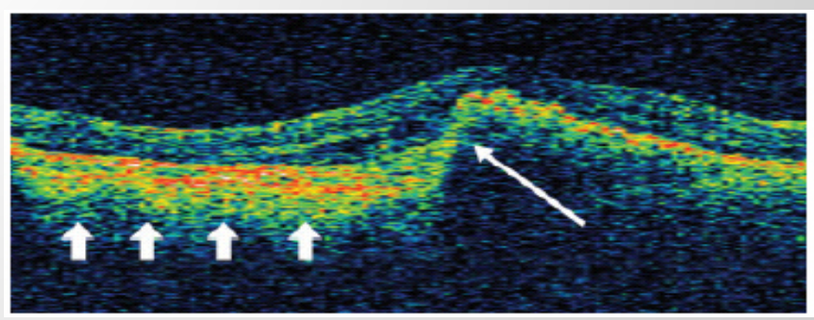
Manoj SM. Why does anti-VEGF treatment fail in AMD. Kerala Journal of Ophthalmology. 2011.

ANTİ-VEGF TEDAVİDE KOMPLİKASYONLAR

<u>Görme Kaybı (%11.6)</u>

- RPE yırtığı,
- RPE atrofisi,
- Skar oluşumuna bağlı





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Doguizi S, **Ozdek S**. PIGMENT EPITHELIAL TEARS ASSOCIATED WITH ANTI-VEGF THERAPY: Incidence, Long-term Visual Outcome, and Relationship with Pigment Epithelial Detachment in Age-related Macular Degeneration. **Retina. 2014** Jun;34(6):1156-62.

PIGMENT EPITHELIAL TEARS ASSOCIATED WITH ANTI-VEGF THERAPY

Incidence, Long-term Visual Outcome, and Relationship with Pigment Epithelial Detachment in Age-related Macular Degeneration

SIBEL DOGUIZI, MD, SENGUL OZDEK, MD

Purpose: To evaluate the prevalence of retinal pigment epithelium (RPE) tears associated with anti-VEGF therapy and its relation with retinal pigment epithelial detachment (PED).

Methods: A total of 226 patients with exudative age-related macular degeneration treated with intravitreal anti-VEGF were included retrospectively in the study. The presence of RPE tears; the effect of the presence, height, and duration of PED on the rate of RPE tears; and change in visual acuity during follow-up were recorded.

Results: Among 226 study patients, 28 (12.3%) had RPE tears. The RPE tear rate was significantly higher in patients with vascularized PED (vPED) than in those without PED (19.7% vs. 2.1%; $P < 0.001$). The change in visual acuity after the formation of RPE tear was not statistically significant (on logMAR scale: 0.92 ± 0.49 initially, 0.89 ± 0.41 after the RPE tear, 0.96 ± 0.45 at the last follow-up; $P = 0.613$). Pigment epithelial detachment height >580 μm (odds ratio = 69.4; 95% confidence interval = 16.7–288.1) and PED duration ≤4.5 months (odds ratio = 166.7; 95% confidence interval = 15.2–1000) were found to be significant risk factors for RPE tear formation.

Conclusion: The RPE tears are not infrequent among eyes treated with intravitreal anti-VEGFs. The presence, increased height, and shorter duration of vPED are potential risk factors for RPE tears associated with anti-VEGF therapy.

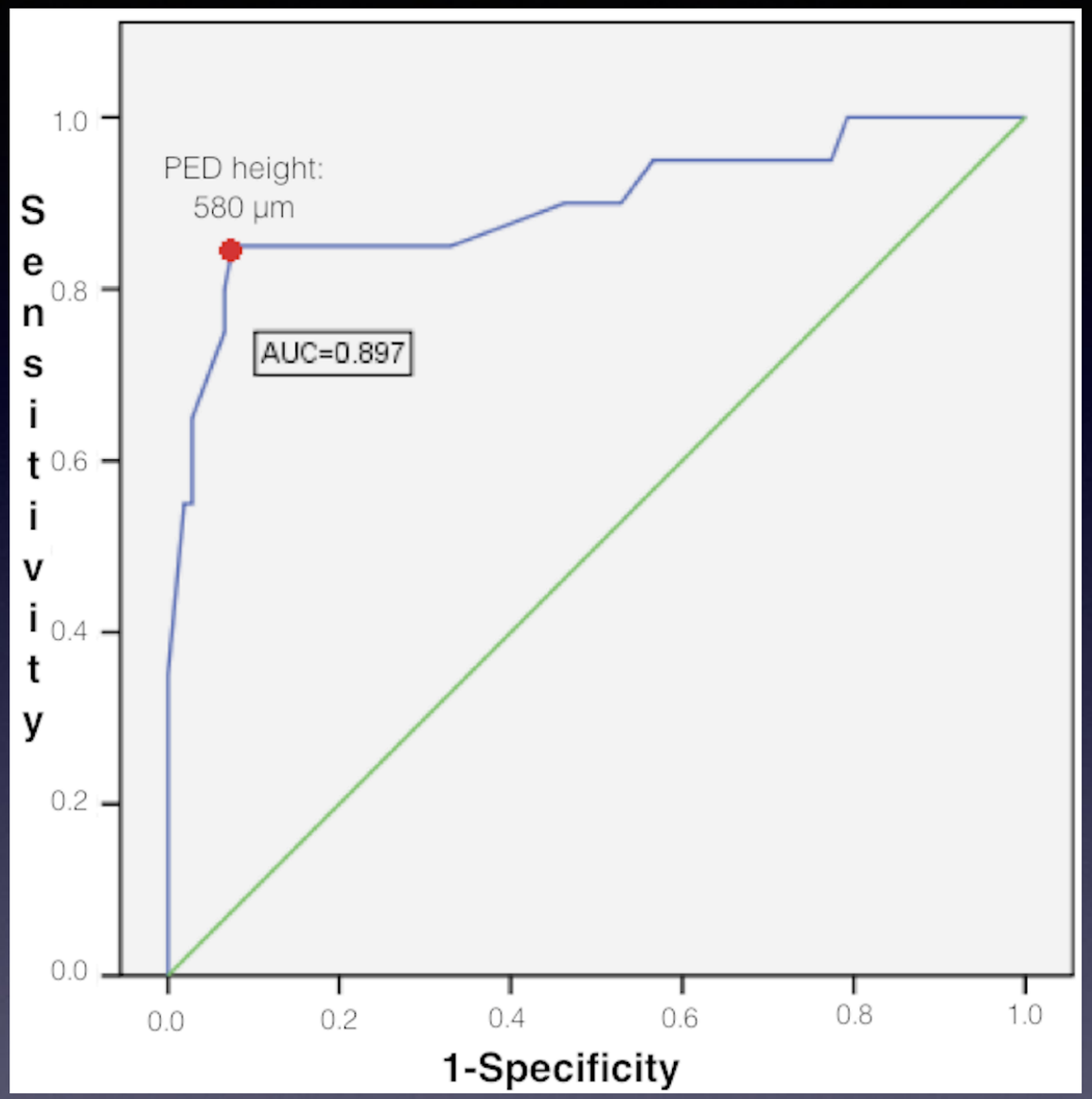
RETINA 0:1–7, 2013

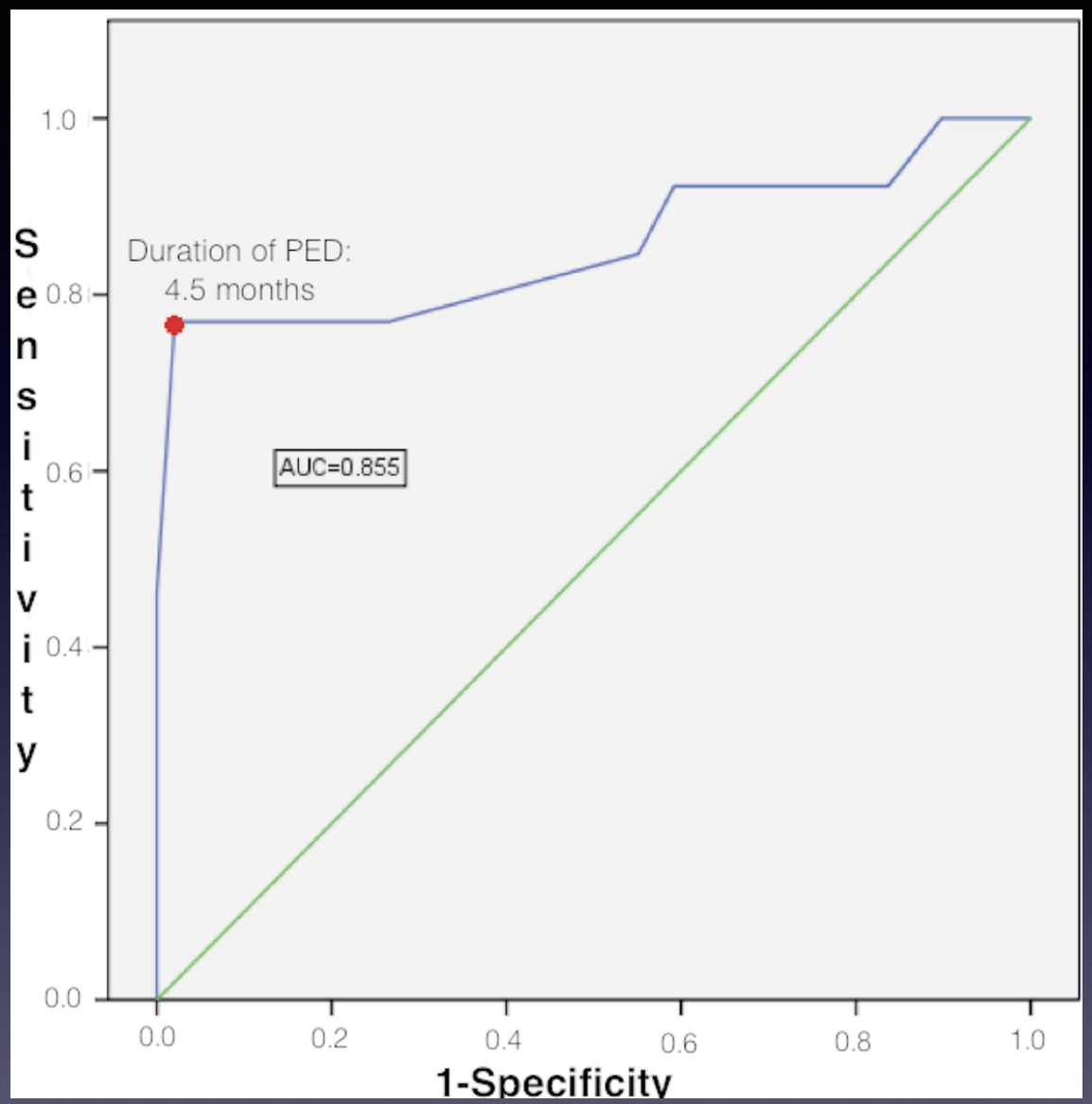
ANTİ-VEGF TEDAVİDE KOMPLİKASYONLAR

RPE Yırtıkları - Anti-VEGF

- Retrospektif analiz: 226 neovasküler YBMD hastası, anti-VEGF tedavisi
- RPE yırtık oranı; 28 göz (12.3%)
- RPE yırtık oranı PED li gözlerde (%19.7) PED siz gözlere göre (%2.1) daha fazla ($p<0.0001$).
- Takipte görmedeki değişimler

PED Büyüklüğü&Süresi-RPE yırtığı





PED yüksekliği >580 µm, ve PED süresi ≤4.5 ay: RPE yırtığı oluşmasında risk faktörleri.

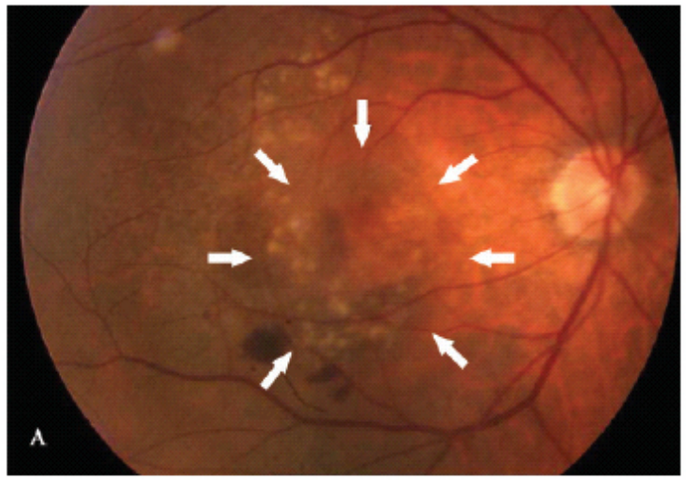
*PED duration predicts RPE tear risk with 77% sensitivity and 98% specificity.

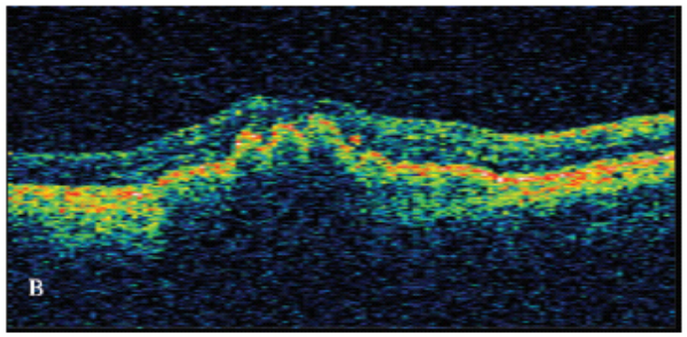
*PED height predicts RPE tear risk with 85% sensitivity and 92% specificity

PED süresi

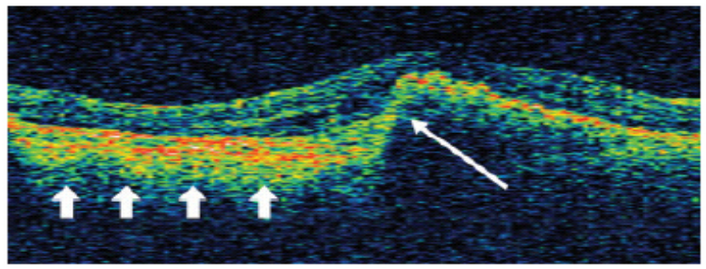
- RPE yırtığı ile ilişkisini gösteren ilk çalışma
- Neovasküler olay taze: immatür damarlar
- Anti-VEGF lere daha hassas,
- Anti-VEGF tedavi cevabı daha dramatik
- KNV'nin kontraksiyonu.....RPE yırtığı!

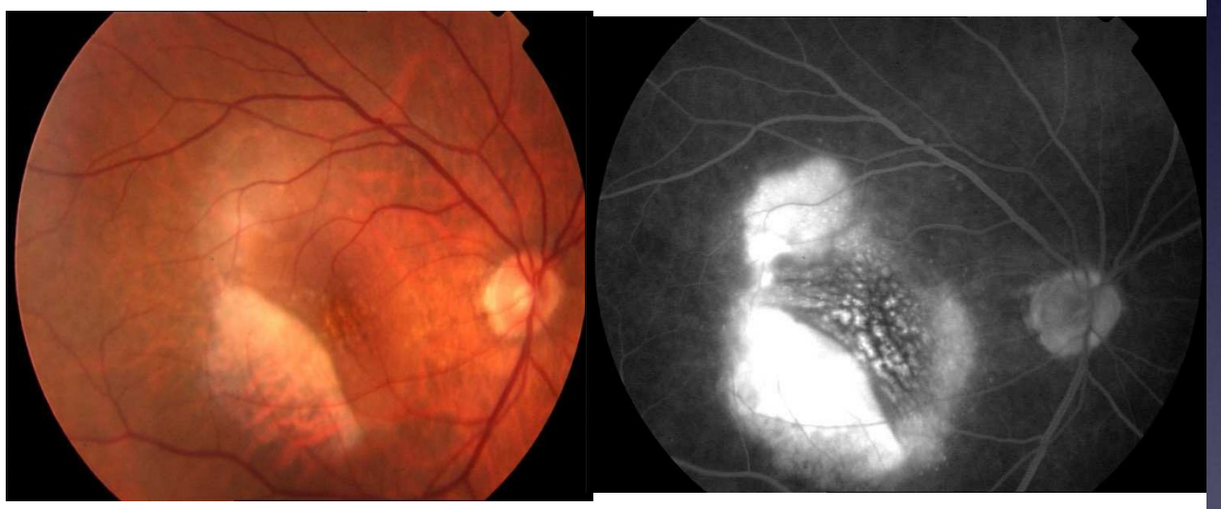
GK: 0.3, Avastin, 2 hf sonra: RPE yırtığı

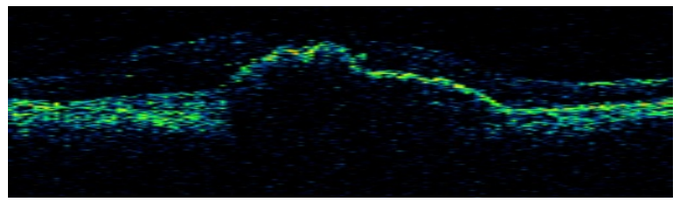








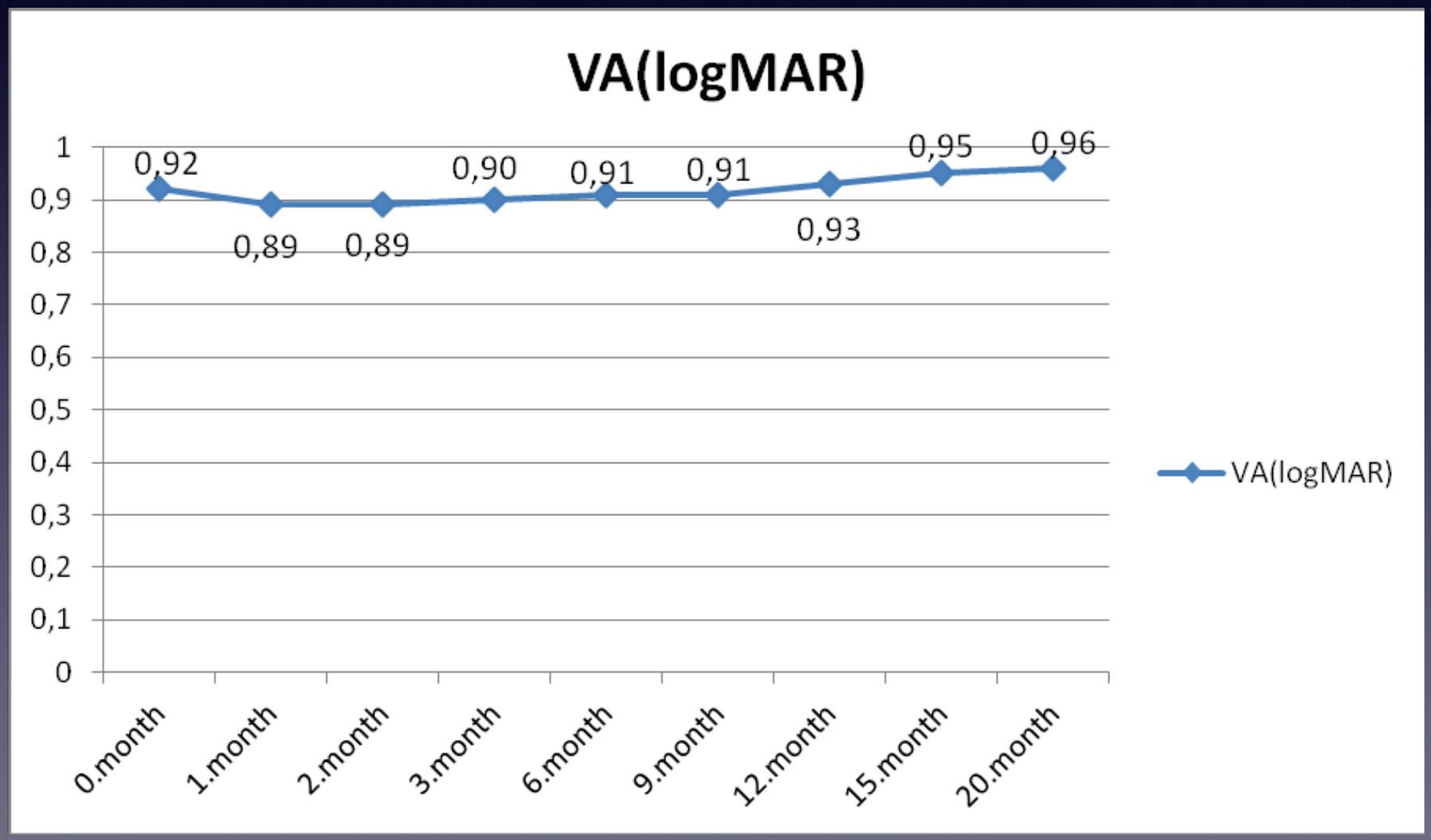




3x Avastin, GK: 0.3

PROGNOZ

- Major belirleyici: foveal tutulum sonucu RPE siz çıplak santral fovea varlığı




VA: 0.3/0.6


EL, 01.01.1947
] ART(9) Q: 24

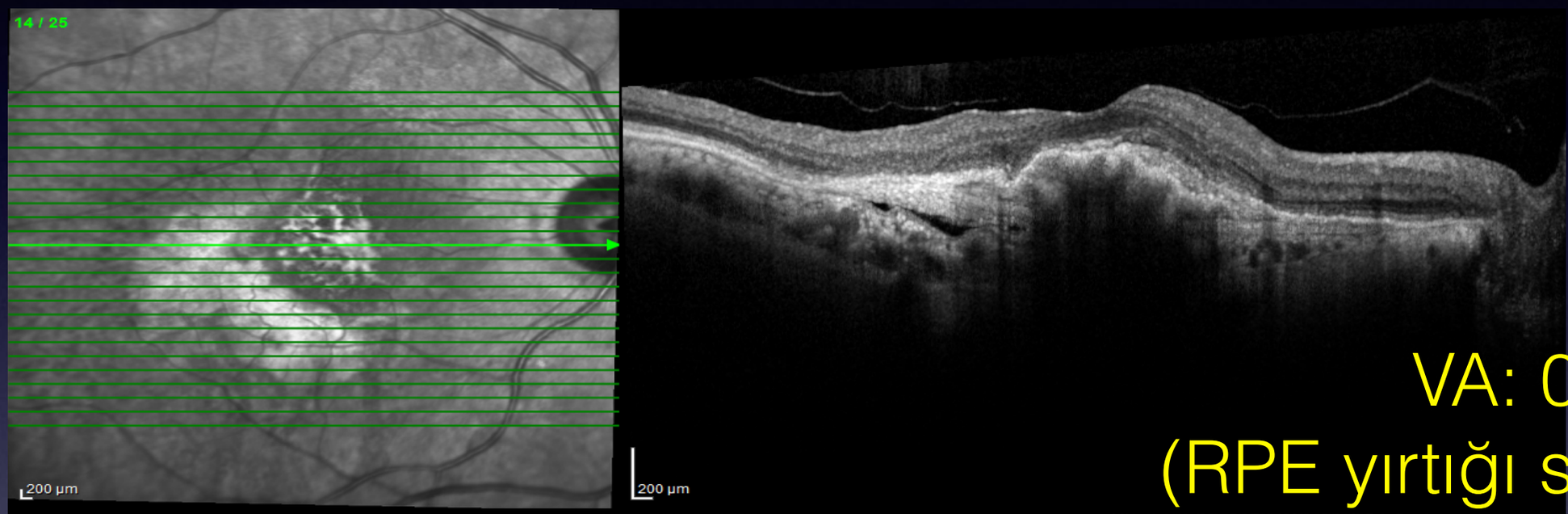

HEIDELBERG
ENGINEERING


VA: 0.3/0.4
200 µm
KURTULUS, EMEL, 01.01.1947
19.09.2014, OD
BAF 30° ART(23)


200 µm
KURTULUS, EMEL, 01.01.1947
19.09.2014, OS
BAF 30° ART(40)
HEIDELBERG
ENGINEERING

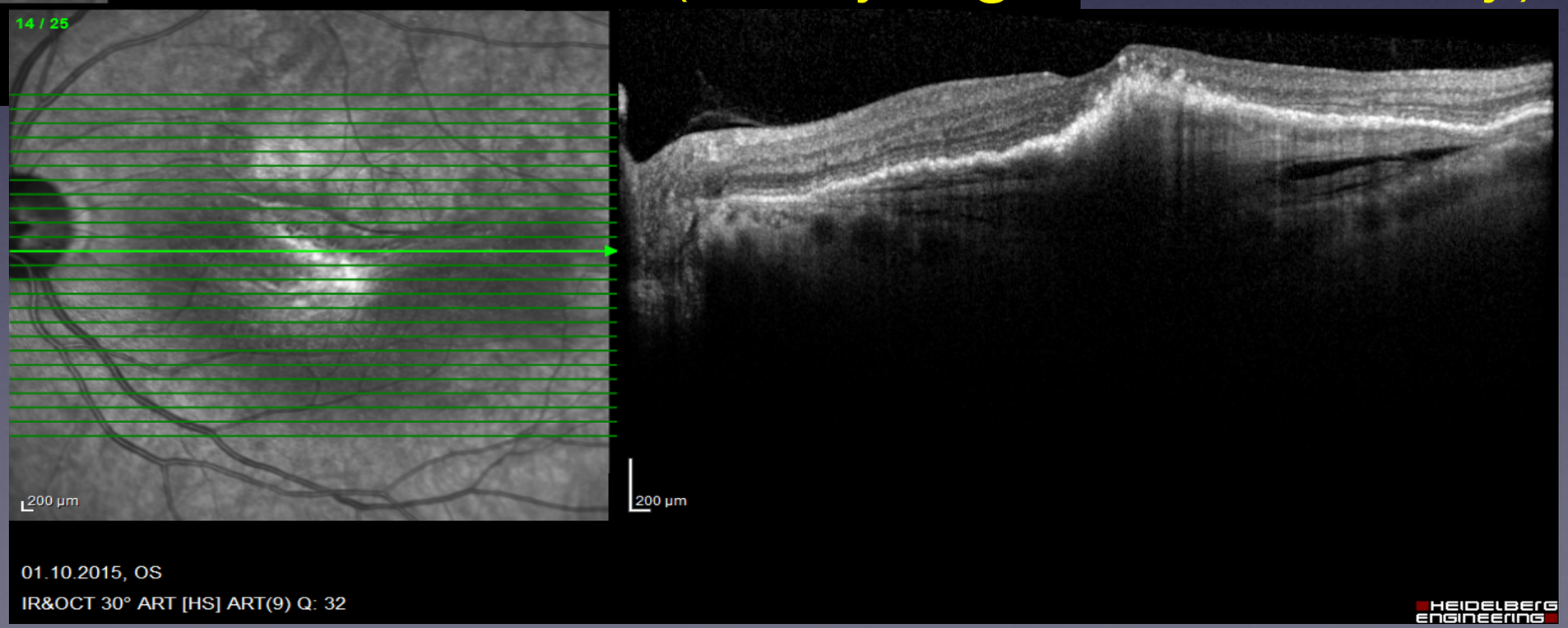
RPE YIRTIĞI

Anti-VEGF tedavisine devam edildi



VA: 0.6/0.7

(RPE yırtığı sonrası 13. ay)



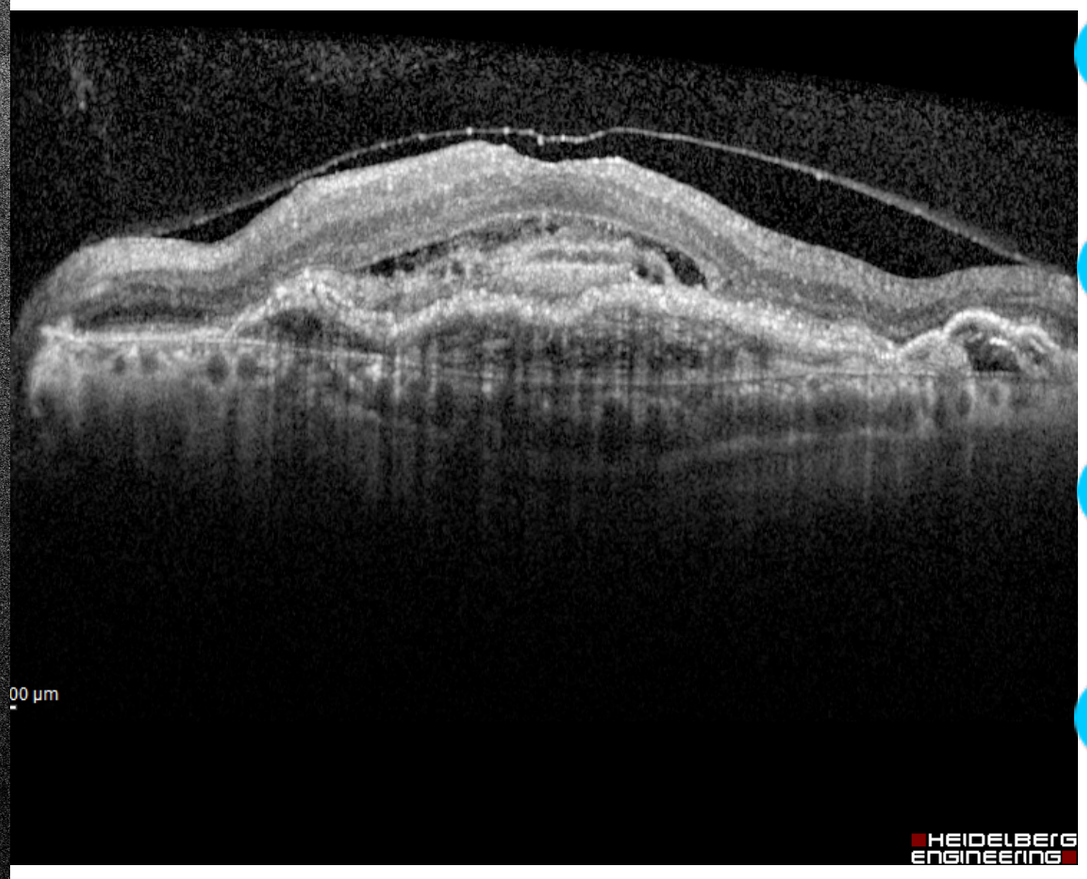
RPE YIRTIĞI

- Fovea çıplak kalmadıkça, devam eden Anti-VEGF tedavi ile iyi sonuç!
- Yüksek PED ve Taze PED: Risk daha yüksek!

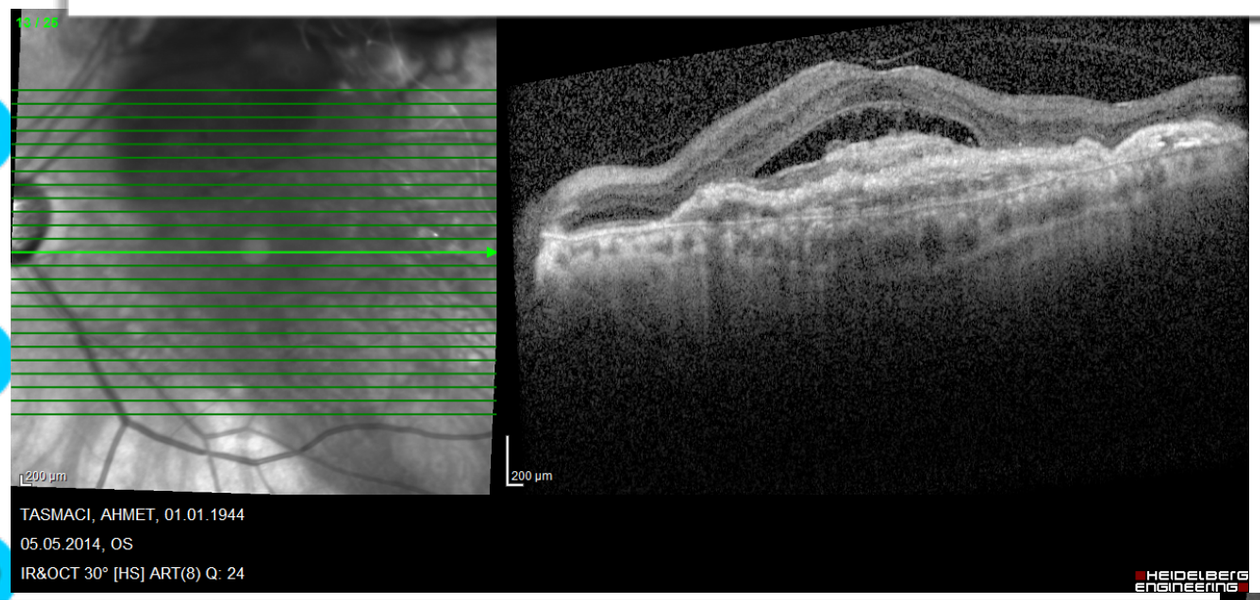
ANTİ-VEGF TEDAVİDE KOMPLİKASYONLAR
FİBROZİS-SKAR

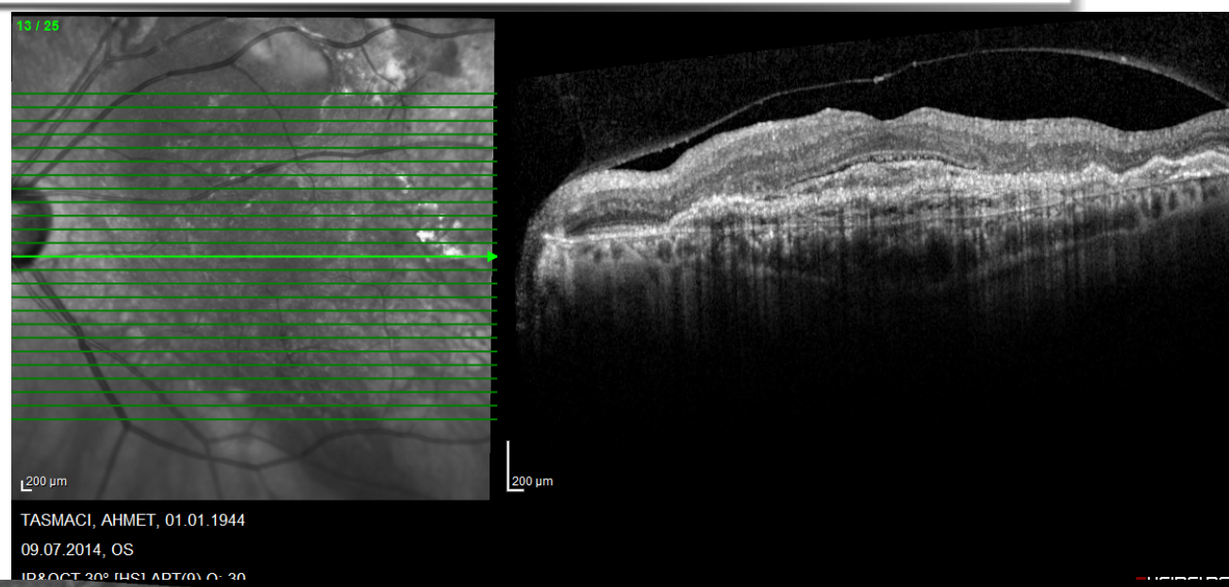


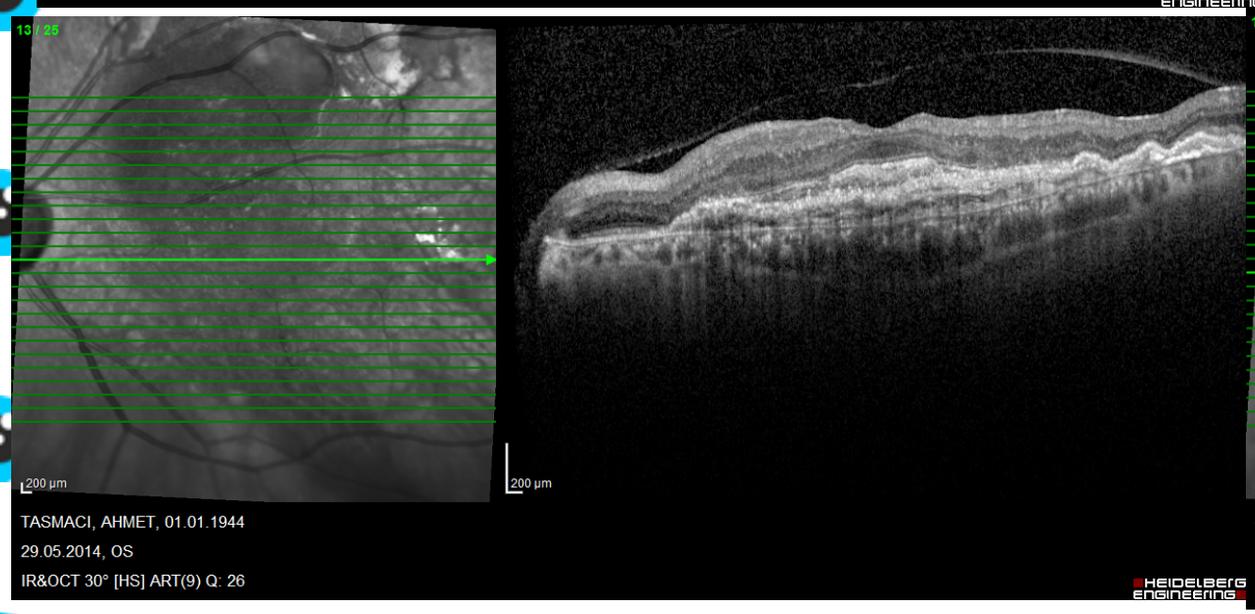
VA: 0.4

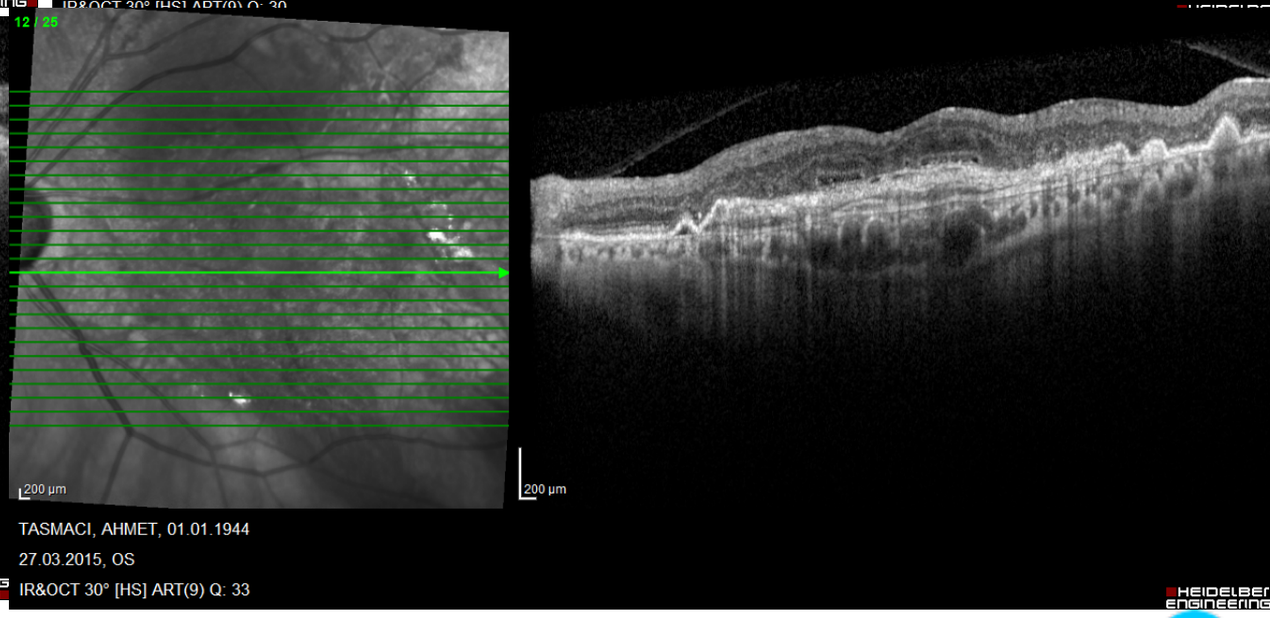


ANTİ-VEGF TEDAVİDE KOMPLİKASYONLAR
FİBROZİS-SKAR









VA↓: 0.05

ANTİ-VEGF TEDAVİDE KOMPLİKASYONLAR
FİBROZİS-SKAR

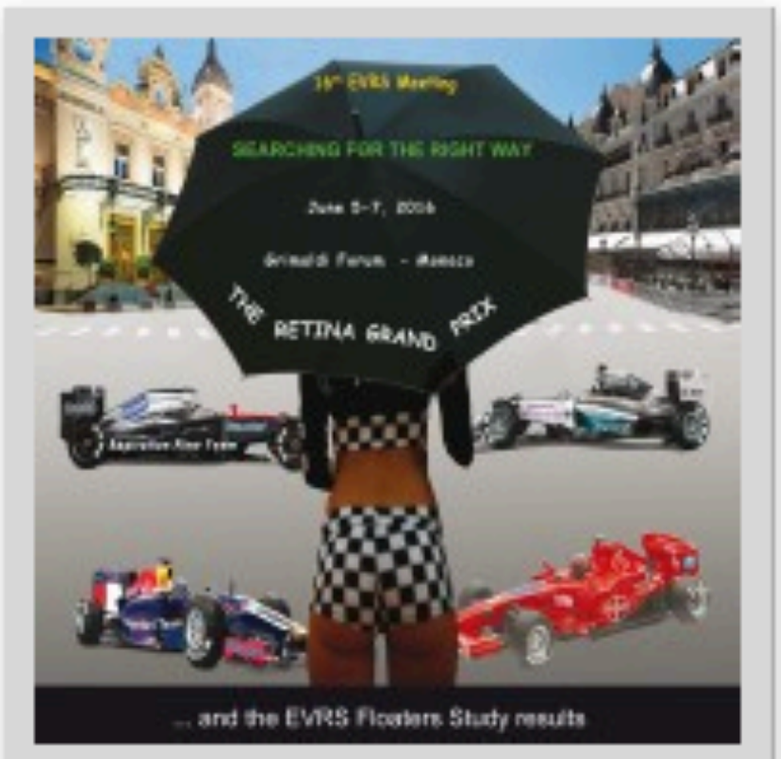


VA↓: 0.05

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2016 Meeting



Abstract Deadline: 10 Ocak 2016

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