

Diabetic Macular Oedema

‘To treat or not to treat?’

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ONE STOP INTRAVITREAL TREATMENT SERVICE 2013

RAPID ACCESS

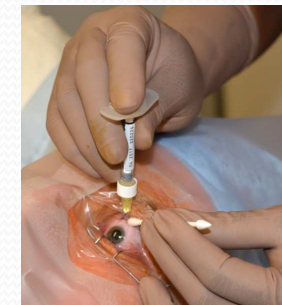
MACULAR DEGENERATION CLINIC

Wet age-related macular degeneration
are seen and treated within two weeks

AMD COORDINATOR

Phone: 01582 497328

Fax: 01582 497956



VISION TESTING

REVIEW OF OCT SCAN

IVT INJECTION

SEE AND TREAT MEDICAL RETINA SERVICE

GP OR OPTOMETRIST REFERRAL



VISION TESTING



REVIEW OF OCT SCAN



IVT INJECTION



FFA



LASER

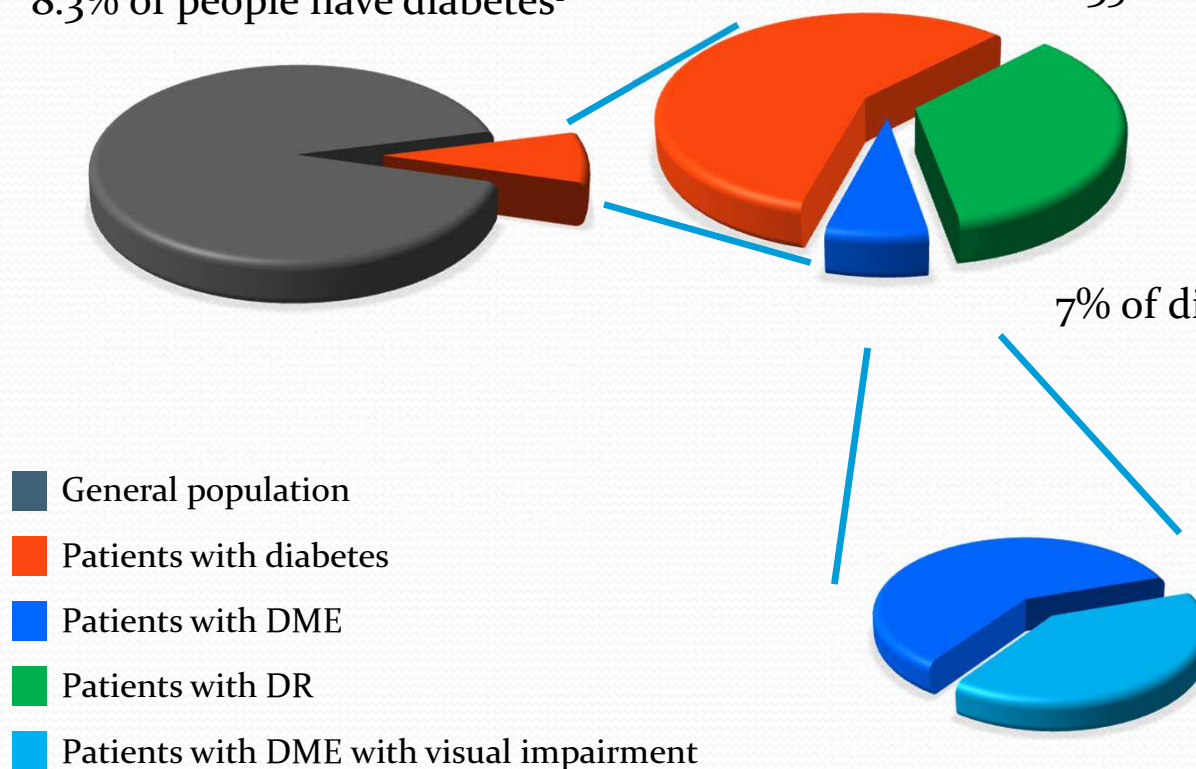


UVEITIS SERVICE

- **UVEITIS CLINIC Monday 1.30 – 5.00 pm**
- **URGENT OR ROUTINE REFERRALS**
- NHS secretary
Sally Bargery:
Email: sally.bargery@ldh.nhs.uk
Phone: 01582 497329
- Private secretary
Angela Sborgia
Email: angela@ranjitsandhu.co.uk
Phone: 0800 042 0258

DMO: commonest cause of visual impairment

8.3% of people have diabetes¹



35% of diabetic patients have DR²

7% of diabetic patients have DME^{2,3}

40% of DME patients have associated visual impairment³

DME, diabetic macular edema
DR, diabetic retinopathy

1. IDF Diabetes Atlas. 5th Edition: <http://www.idf.org/diabetesatlas/5e/the-global-burden> [Accessed 26 July 2013];
2. Yau J, et al. Diabetes Care 2012;35:556-64
3. Minassian D, et al. Br J Ophthalmol 2012;96:345-9

Co-morbidities

Co-morbidities

- HbA_{1c}: 48-58 mmol/l (6.5-7.5%)
Rosiglitazone and pioglitazone should be avoided if macular oedema
- BP: <130/80 (<125/75 if protein in urine). NB: ACE-inhibitors
- Lipids: Total cholesterol <4mmol/l. Consider adding Fenofibrates
- Control sleep apnoea



Lifestyle

- Exercise (metabolic memory)
- Avoid obesity
- Avoid smoking
 - Smoking X3-4 retinopathy
- Moderate alcohol consumption only

Metabolic memory/Legacy effect

Evidence for prevention

- ¹United Kingdom Prospective Diabetes Study (UKPDS)
- ²Diabetes Control and Complications Trial (DCCT)

BP: <130/80 (<125/75 if protein in urine)

HbA_{1c}: 48-58 mmol/l (6.5-7.5%)

Lipids: Total cholesterol <4mmol/l.

1. UKPDS Study Group. Lancet. 1998. Volume 352, No. 9131; p837-853,

2. DCCT Study Group. The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus
NEJM. 1993; 329:977-986

Important definitions

Diabetic Retinopathy Screening (DRSS)

M0

Not M1

Microaneurysm or dot haemorrhage
 ≤ 1 Disc Diameter from central fovea, VA $\leq 6/12$

M1

Exudate/thickening ≤ 1 DD from central fovea

Circinate or group of exudates within the macula (circle with radius from fovea to disc)

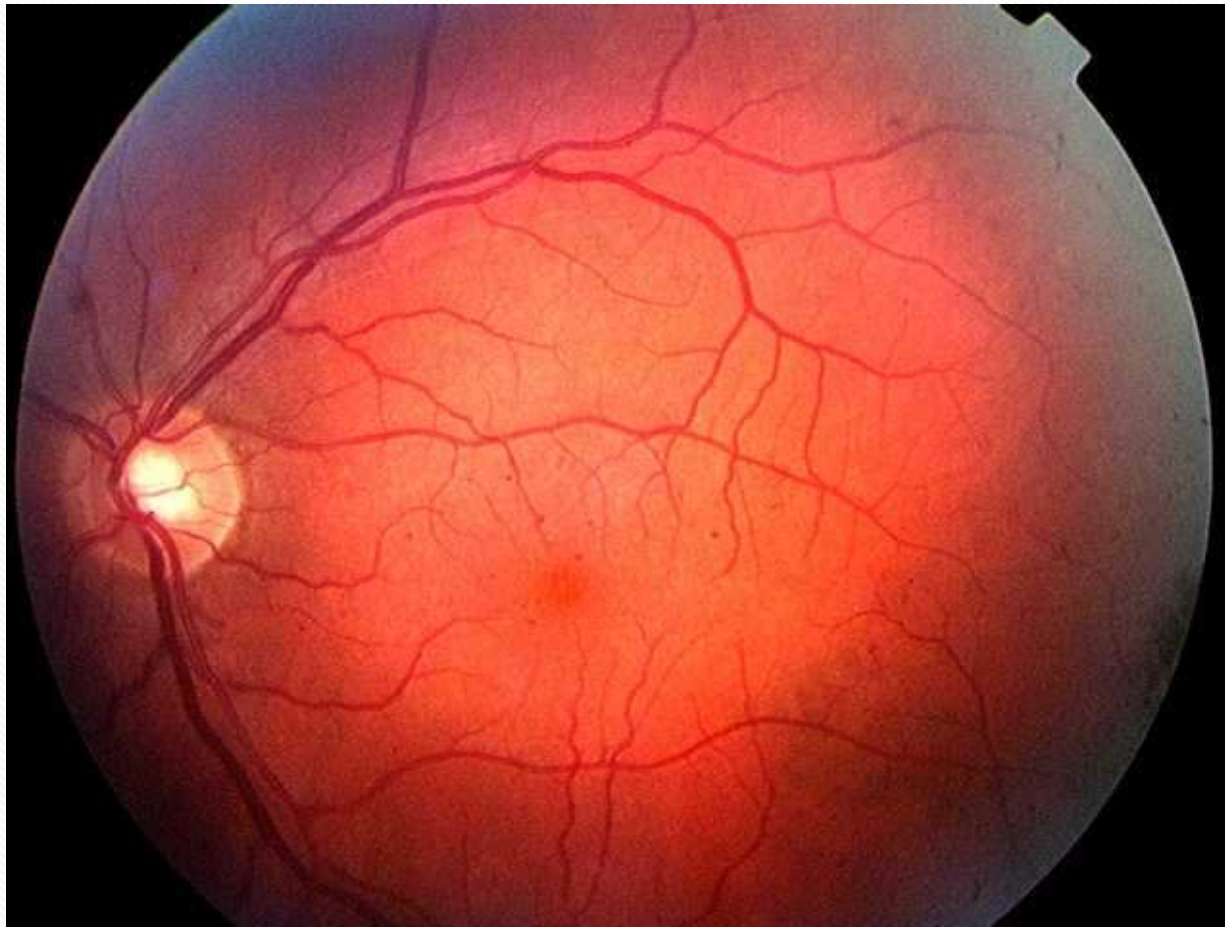
Clinically Significant Macular Oedema (CSMO)

Any thickening within 500 μ m of central fovea

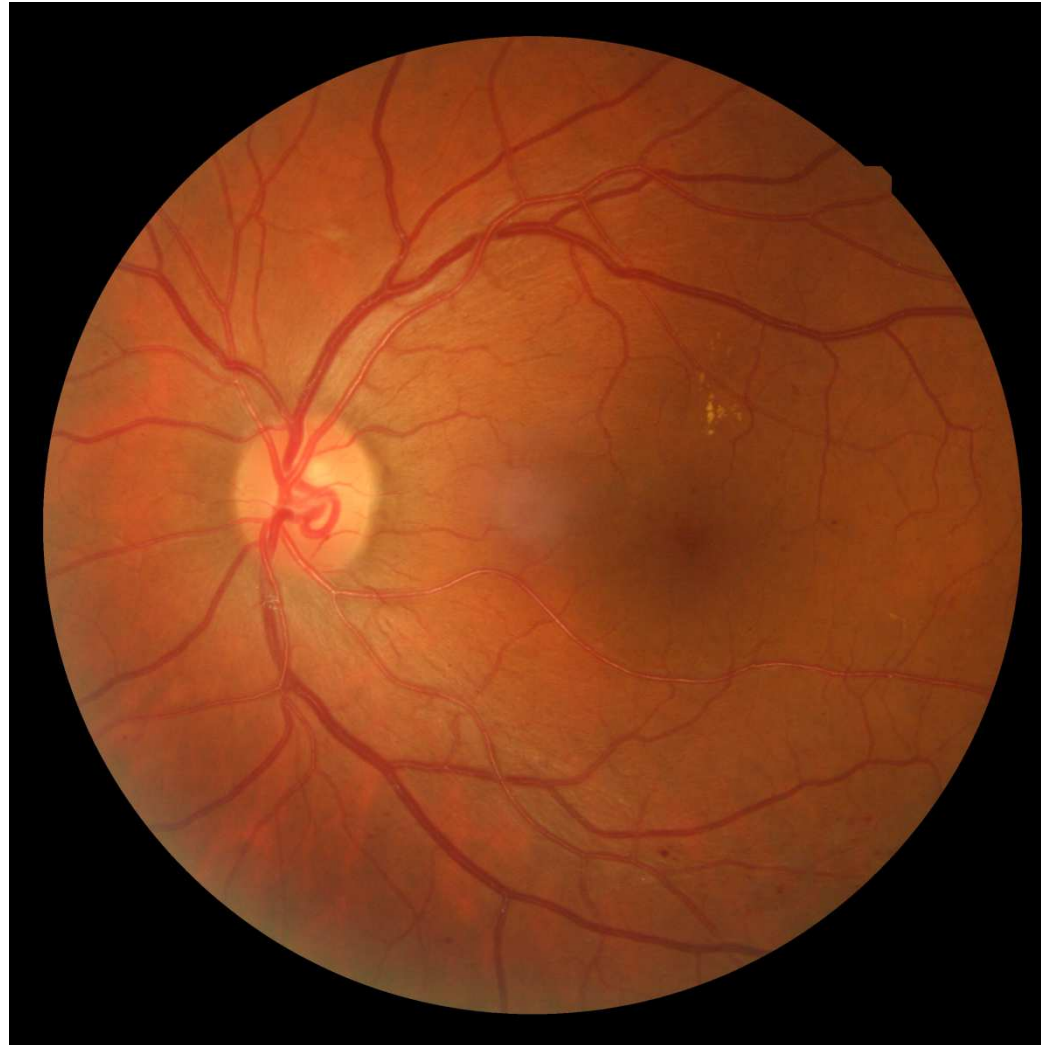
Exudate within 500 μ m of central fovea, with adjacent thickening

Thickening of 1 disc area, ≤ 1 DD from central fovea

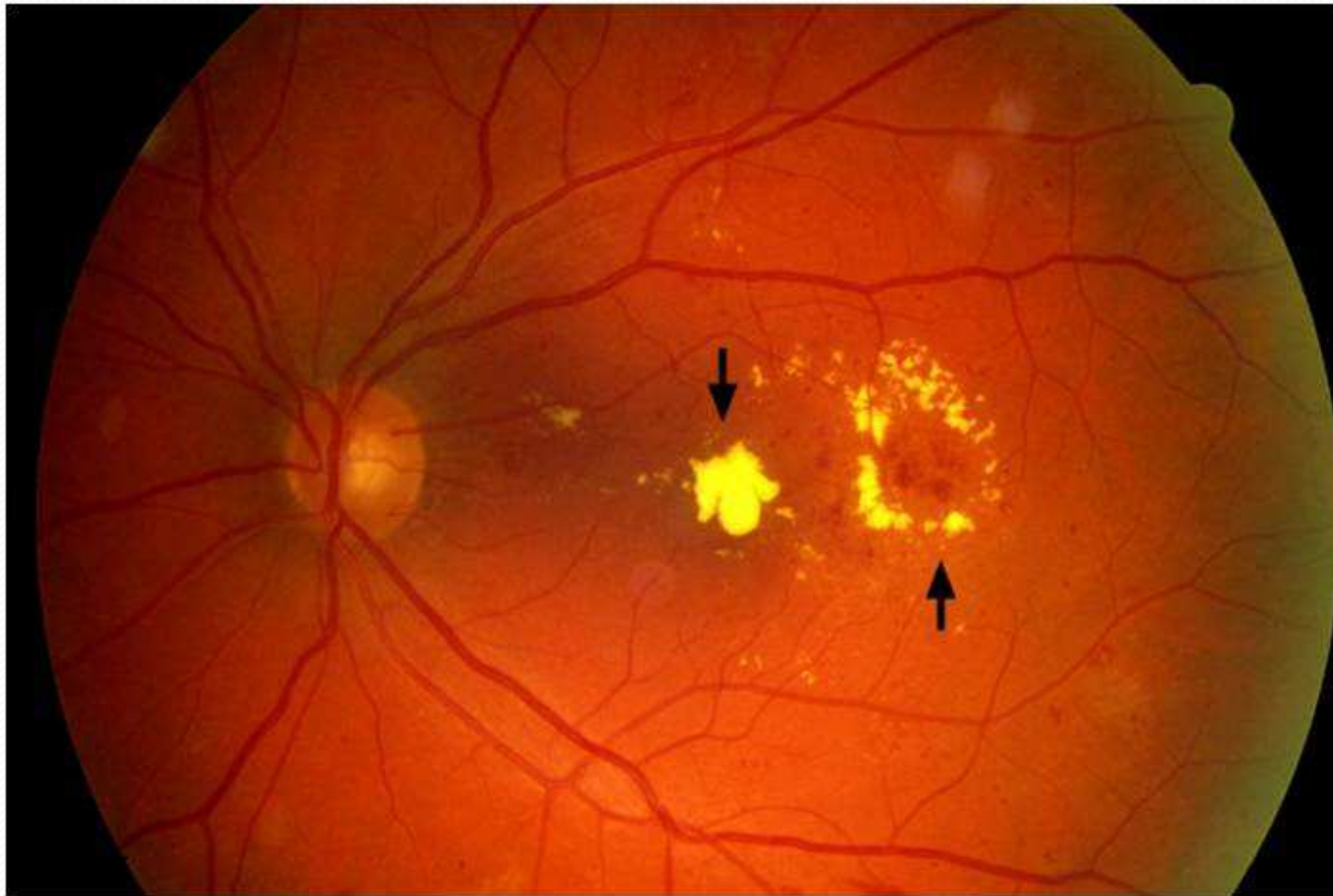
What's the DRSS grading? M0 or M1



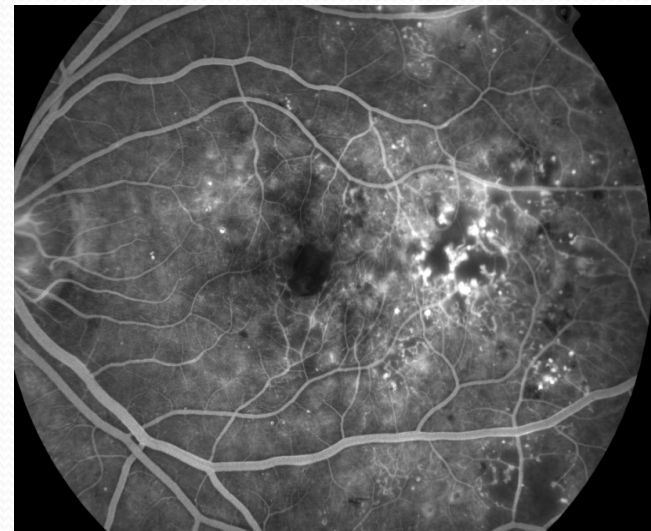
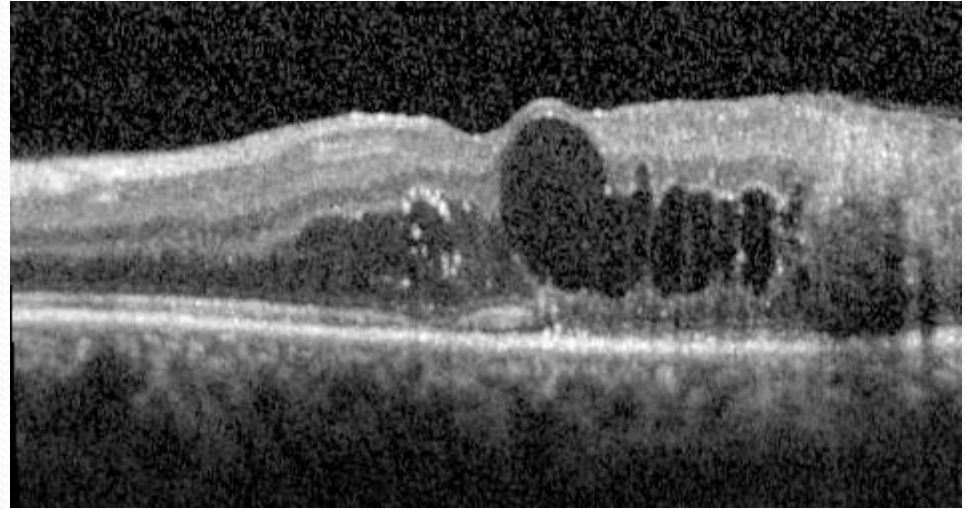
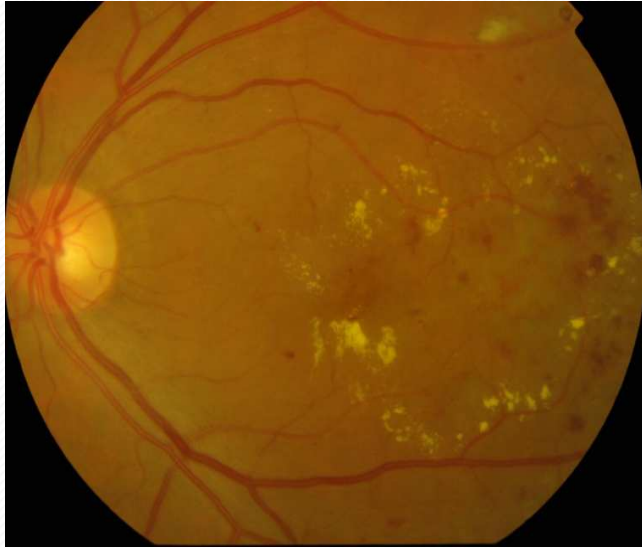
What's the DRSS grading? M0 or M1



What's the DRSS grading? M0 or M1



DMO



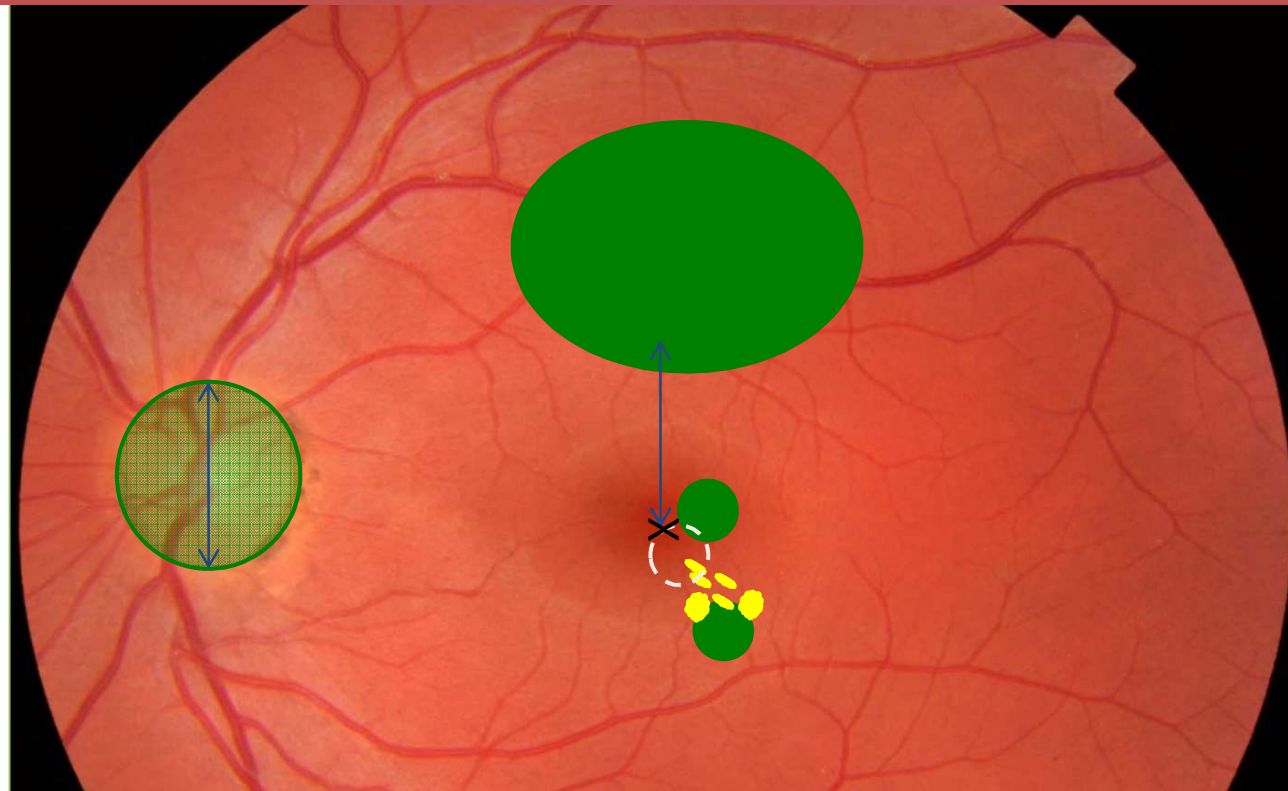


Diabetic Macular Oedema

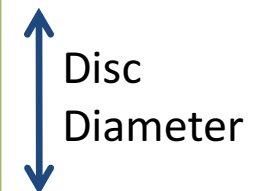
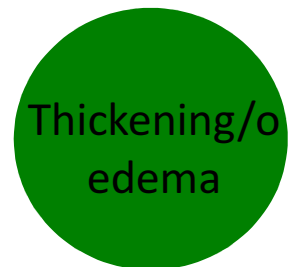
- Laser
- Intravitreal Triamcinolone
- Anti-VEGF (Ranibizumab/Lucentis)
- Fluocinolone implant (Iluvien)
- Dexamethasone implant (Ozurdex)

1. The Diabetic Retinopathy Clinical Research Network. *Ophthalmology* 2010; 117:1064–77;
The Diabetic Retinopathy Clinical Research Network
2. MEAD Study Group: Boyer DS et al. *Ophthalmology* 2014, 121, 1904-1914
3. FAME Study Group: Campchiaro PA et al. *Ophthalmology* 2012, 119:2125–21321

Clinically significant macular oedema (CSMO)



× Macula centre



(---) 500µm radius



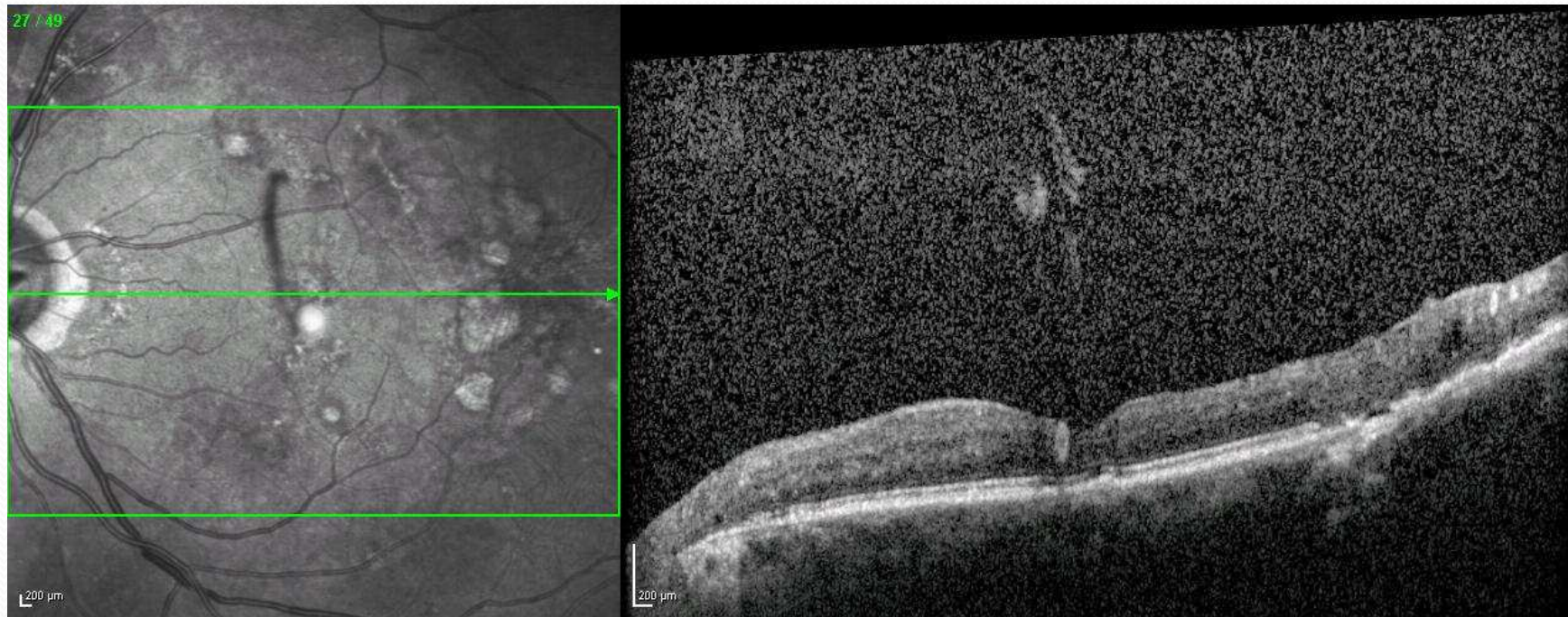
Clinically Significant Macular Oedema (CSMO)

- Thickening of 1 disc area, ≤ 1 DD from central fovea
- Exudate within 500µm of central fovea, + adjacent thickening
- Any thickening within 500 µm of central fovea

CASE 1 – Mr ED

- 1998: 75 year old Caucasian gentleman
- History of diabetes; attended for retinopathy review
- VA RE 6/9 VA LE 6/24
- Examination: Bilateral pseudophakia

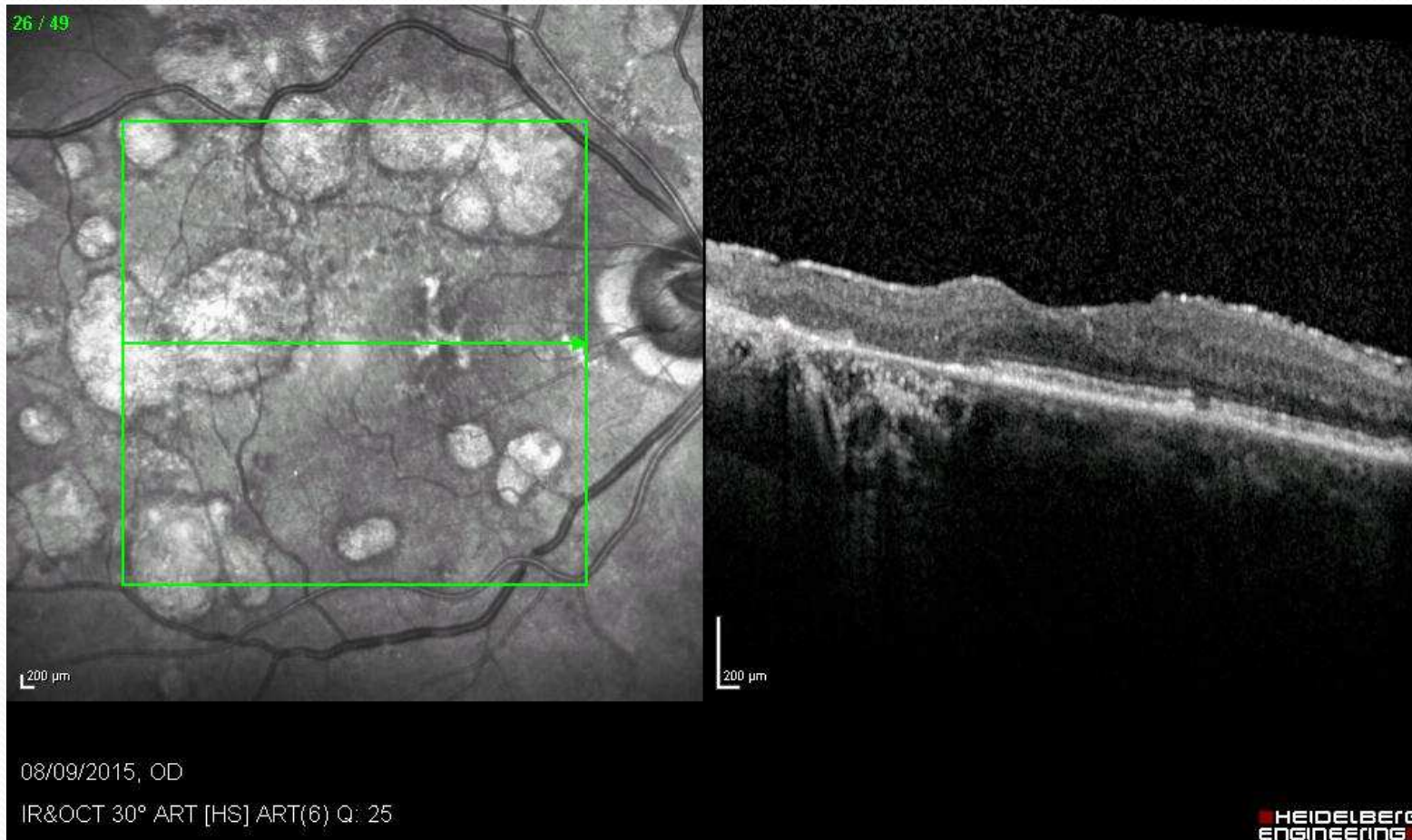
OCT



08/09/2015, OS
IR&OCT 30° ART [HS] ART(5) Q: 19

HEIDELBERG
ENGINEERING

OCT



Options

- Laser treatment in the past

Macular laser – power, spot size, duration, no.

152 x 0.1S x 0.22W x 200 microns

152 x 0.02S x 0.1W x 50-100 microns

- OCT findings

Extensive loss of photoreceptors

No macular oedema

Recurrence of oedema ?

Pharmacological therapy: intravitreal steroid treatment

Corticosteroids have wide-ranging effects

- Affect vascular permeability and angiogenesis¹
- Stabilise the blood–retinal barrier by ↓ cytokines and permeating proteins, including VEGF²

Potential complications of corticosteroid therapy

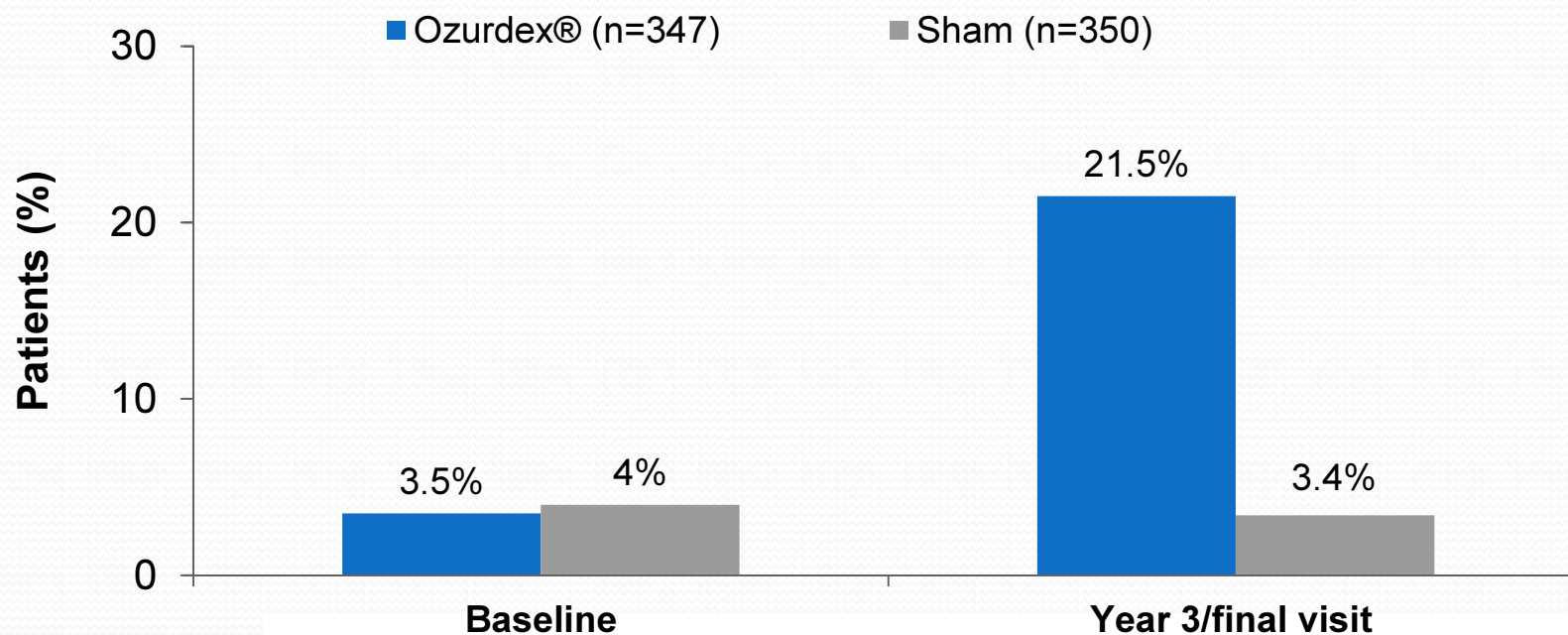
- ↑ IOP seen in ~40% of eyes within 3 months²
- Increased cataract formation which may become visually significant in ~50% of eyes²

1. Mavrikakis and Lam. *Can J Ophthalmol* 2009;44:147–53;

2. Furlani *et al.* *Expert Opin Emerg Drugs* 2007;12:591–603

USE OF IOP LOWERING MEDICATIONS

Use of IOP-lowering medications (safety population)^{1,2}



1. Boyer DS et al. *Ophthalmology* 2014, 121, 1904-1914

2. Adapted from: Allergan data on file. Intraocular pressure; 2014.



Feb 2013 TA274 - Ranibizumab

Lucentis, Novartis. £742.17 per vial 0.5mg/0.05 ml

Ranibizumab is recommended as an option for treating visual impairment due to diabetic macular oedema **only if:**

- central retinal thickness of $\geq 400 \mu$
and
- the manufacturer provides ranibizumab with the discount agreed in the patient access scheme



Nov 2013 TA301 - Flucinolone

Flucinolone, Alimera. £5500 0.2 µg/day/3 years

chronic diabetic macular oedema that is insufficiently responsive to available therapies

only

if the implant is to be used in an eye with an intraocular (pseudophakic) lens **and** the manufacturer provides fluocinolone acetonide intravitreal implant with the discount agreed in the patient access scheme

July 2015 TA346 - Aflibercept

Eylea, Bayer Pharma £816.00 per vial 2mg

The final draft guidance **recommends** aflibercept solution for injection as a treatment option in people **only if:**

- central retinal thickness of $\geq 400 \mu$ and
- the company provides aflibercept with the discount agreed in the patient access scheme.





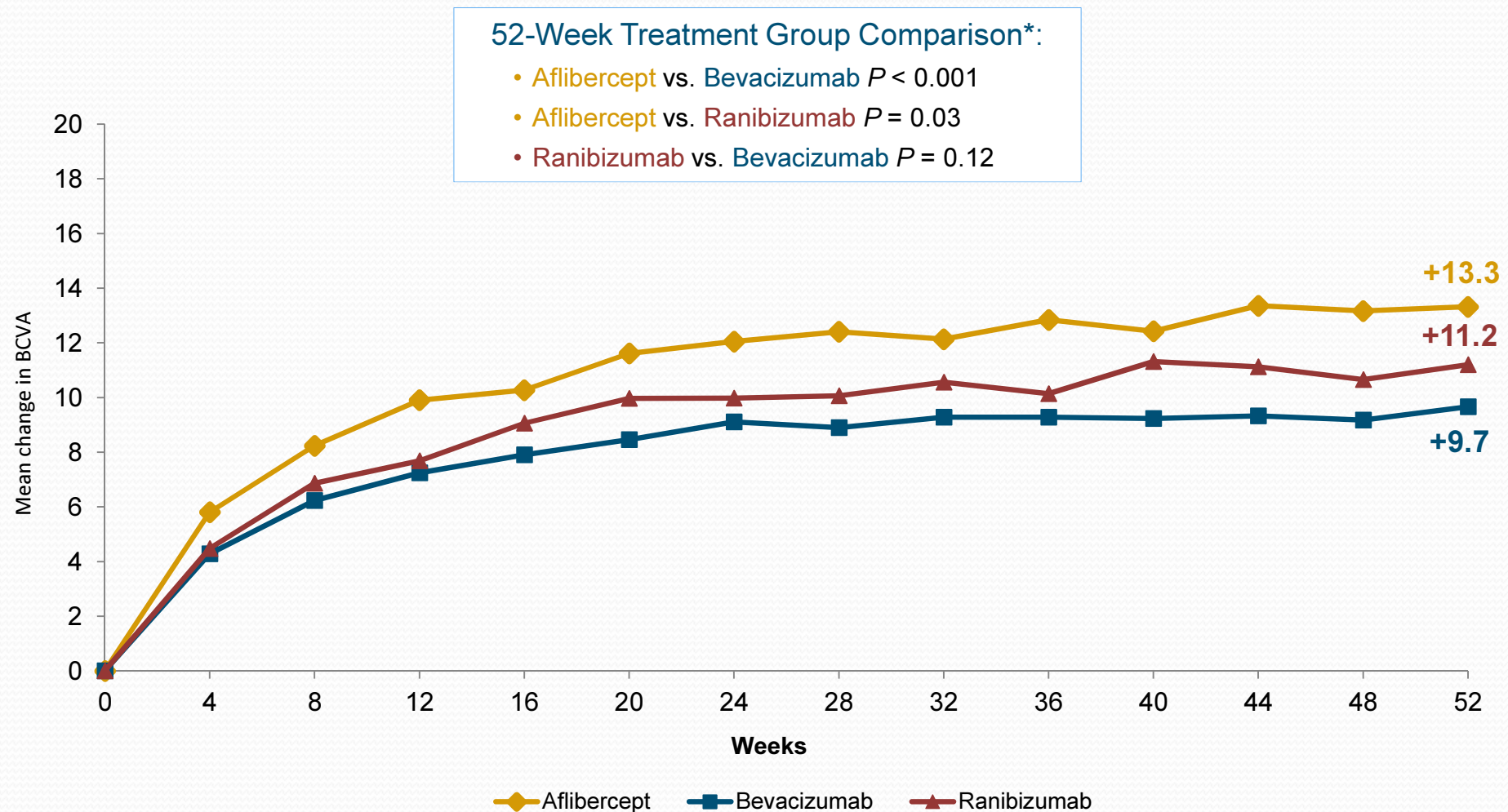
July 2015 TA349 - Dexamethasone intravitreal implant

Ozurdex, Allergan £870.00 per vial 700 micrograms

The final draft guidance dexamethasone intravitreal implant is **recommended** as a treatment option in people **only if**:

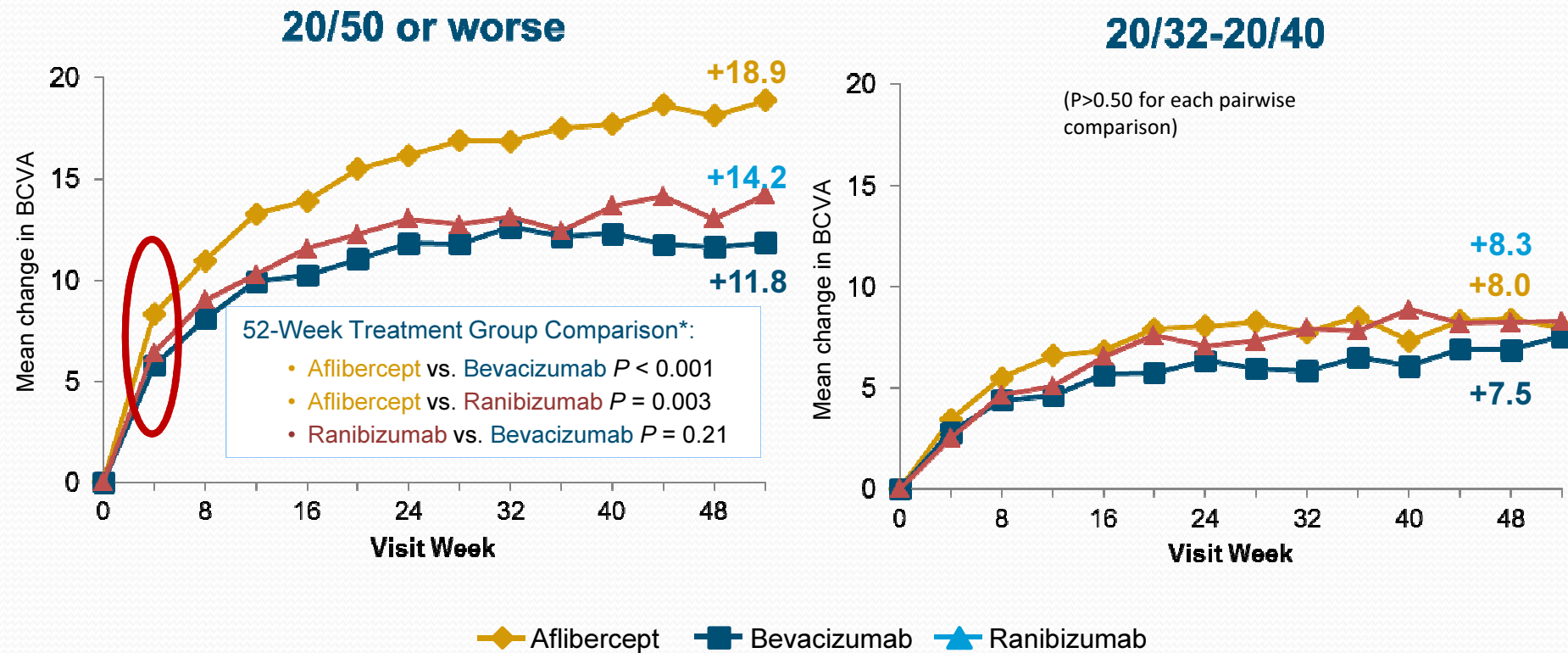
- the implant is to be used in an eye with an intraocular (pseudophakic) lens
and
- their diabetic macular oedema does not respond to non-corticosteroid treatment or such treatment is unsuitable.

Mean Change in Visual Acuity Letter Score Over Time



* P -values adjusted for baseline visual acuity and multiple comparisons.

Subgroup Analysis *Baseline Best-Corrected Visual Acuity*



* P -values adjusted for baseline visual acuity and multiple comparisons.

10- and 15-Letter Gainers at Year 1

	Aflibercept N = 208	Bevacizumab N = 206	Ranibizumab N = 206	P-values for Aflibercept vs. Ranibizumab
Overall (letter score)				
≥10-letter improvement	63%	52%	59%	0.25
≥15-letter improvement	42%	29%	32%	0.068
BCVA 20/50 or worse				
≥10-letter improvement	77%	60%	69%	0.20
≥15-letter improvement	67%	41%	50%	0.008
BCVA 20/32–20/40				
≥10-letter improvement	50%	45%	50%	0.95
≥15-letter improvement	18%	16%	15%	0.73

“(...) improvement in the visual-acuity letter score of at least 15 (3 Snellen lines) was observed in 63% more aflibercept-treated eyes than bevacizumab-treated eyes (67% vs. 41%) and in 34% more aflibercept-treated eyes than ranibizumab-treated eyes (67% vs. 50%).”

BCVA, best-corrected visual acuity. Wells *et al.* *New Engl J Med* 2015.

Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema; The Diabetic Retinopathy Clinical Research Network February 18, 2015

DOI: 10.1056/NEJMoa1414264.

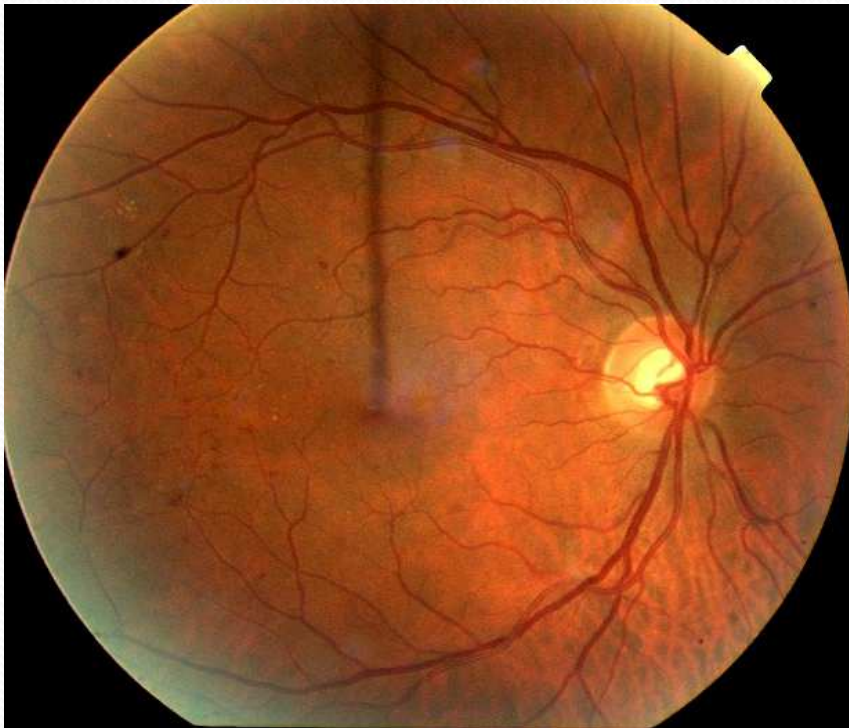
CASE 2 Mrs MT

- 58 year old Asian lady, single mother
- Type 2 Diabetes for 15 years
- PMH -Hypertension, raised Cholesterol
- DH - Vidagliptin, Ramipril, Metformin, Gliclazide

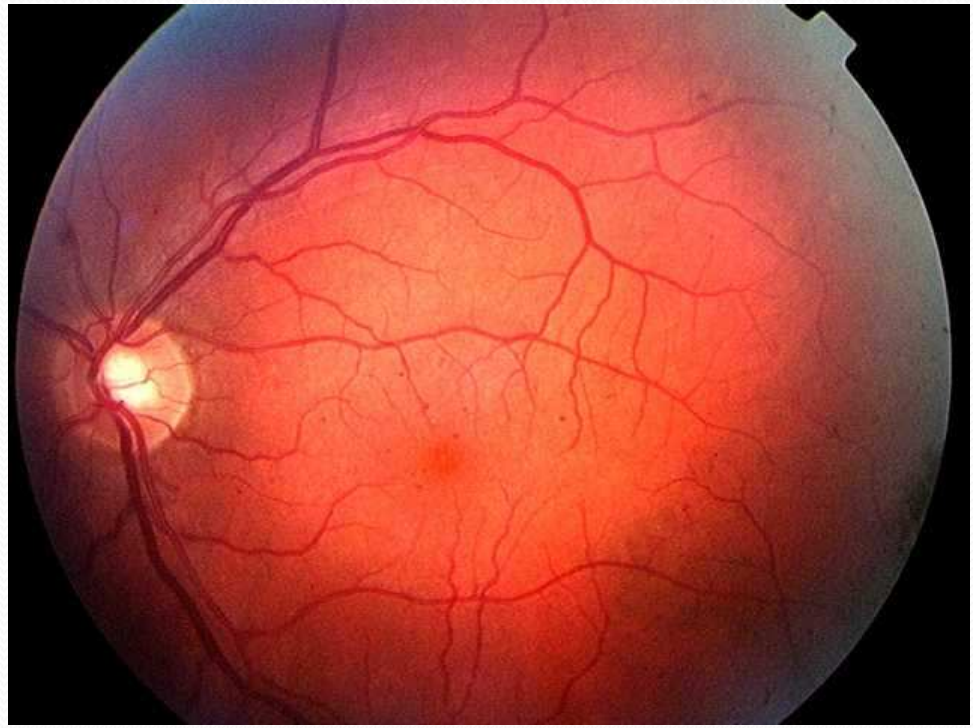
- Referred by DESP
- R₁ M₁
- VA RE 6/5 VA LE 6/18

M1 Maculopathy

VA 6/5

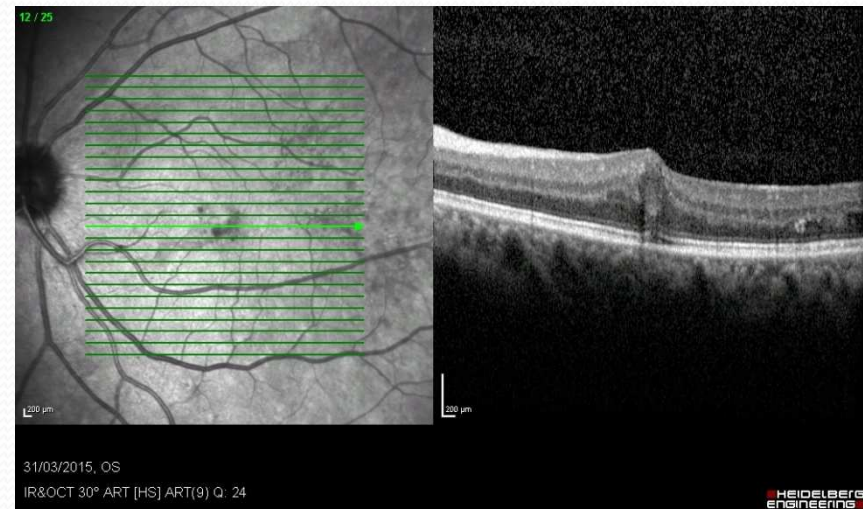
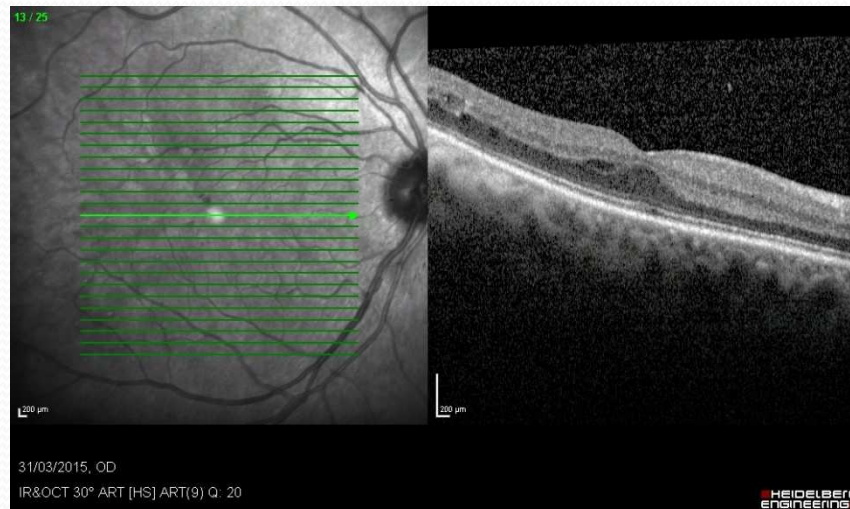


VA 6/18



M1

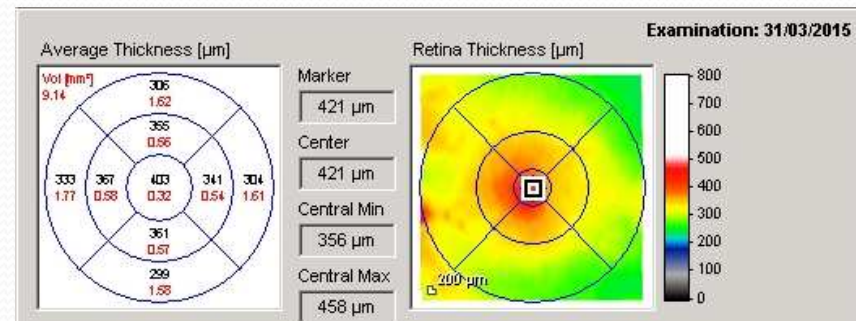
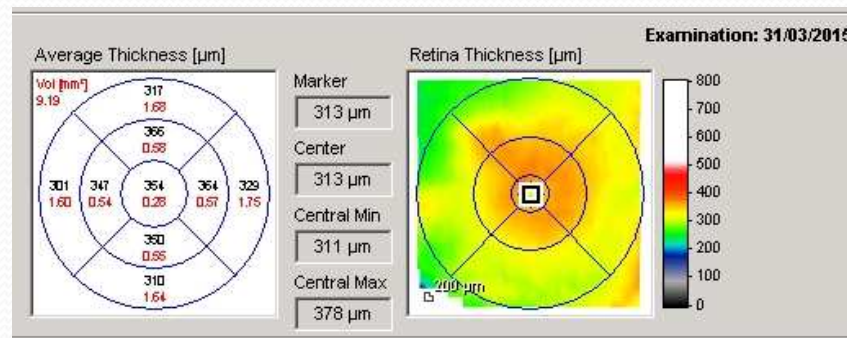
OCT March 2015



CENTRAL MACULAR THICKNESS

354 microns

403 microns

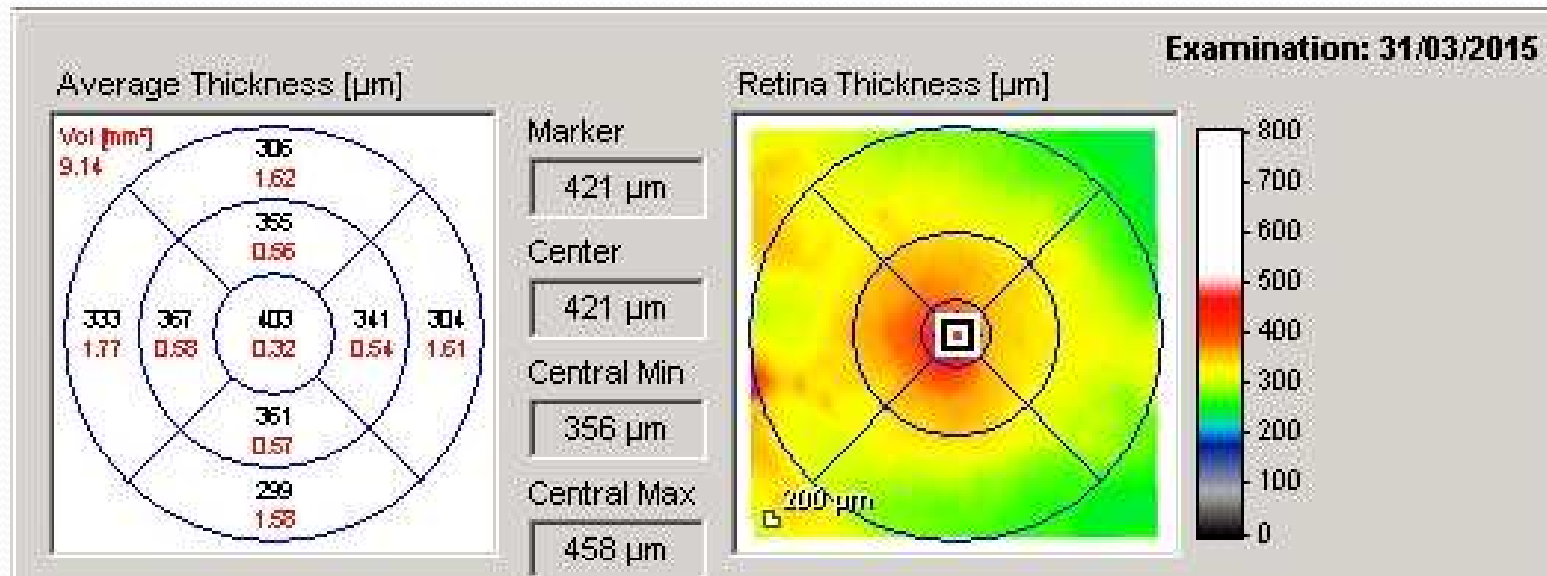
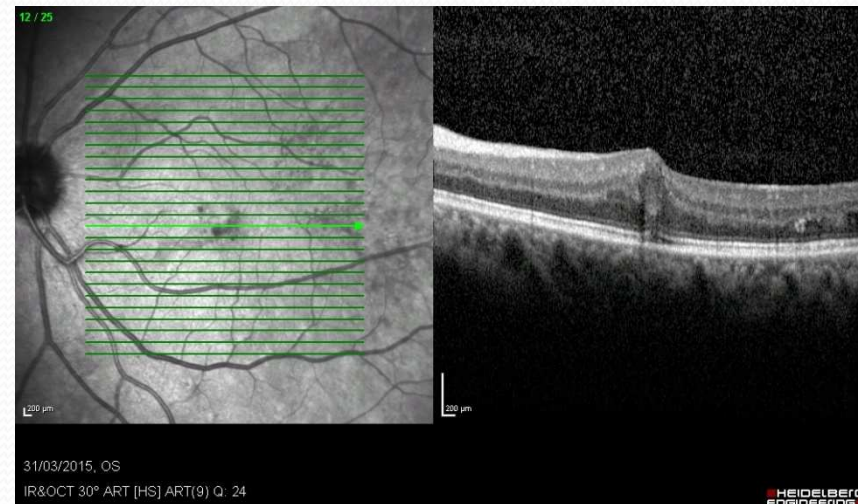


Options RE?

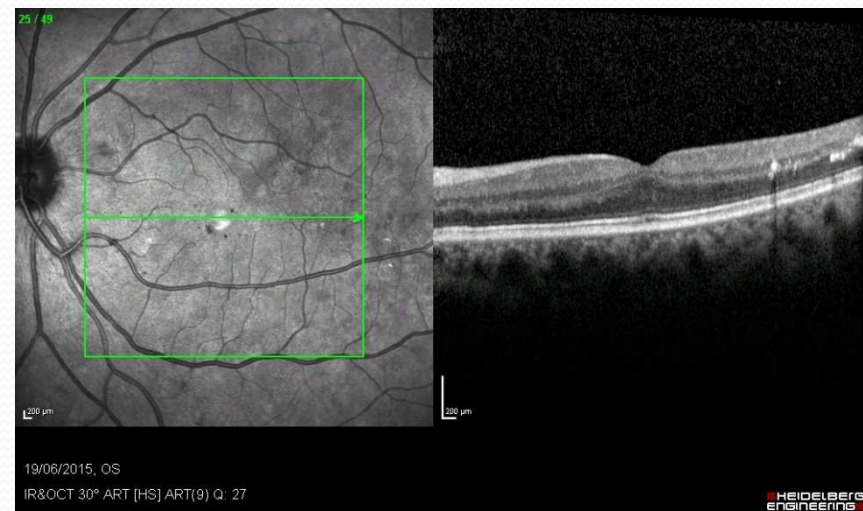
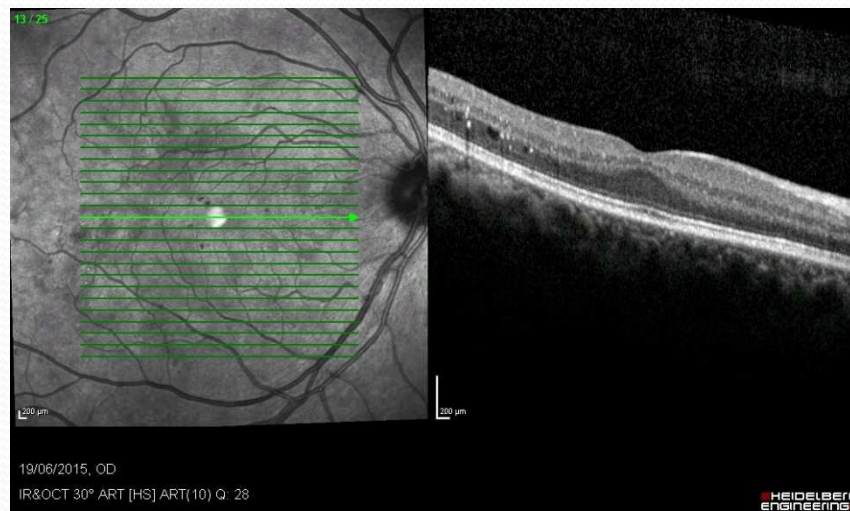
- Control diabetes
- Control BP
- Control hypercholesterolaemia

Options LE?

- Control diabetes
- Hypertension
- Cholesterol
- Anti VEGF?



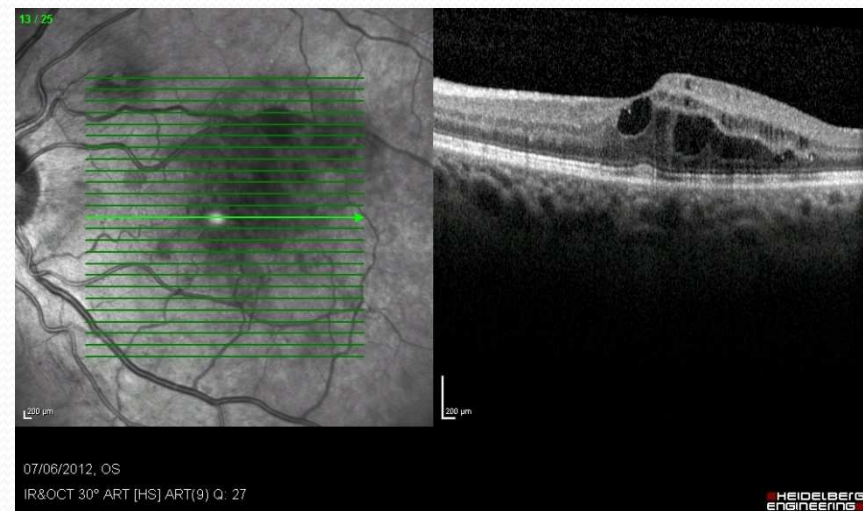
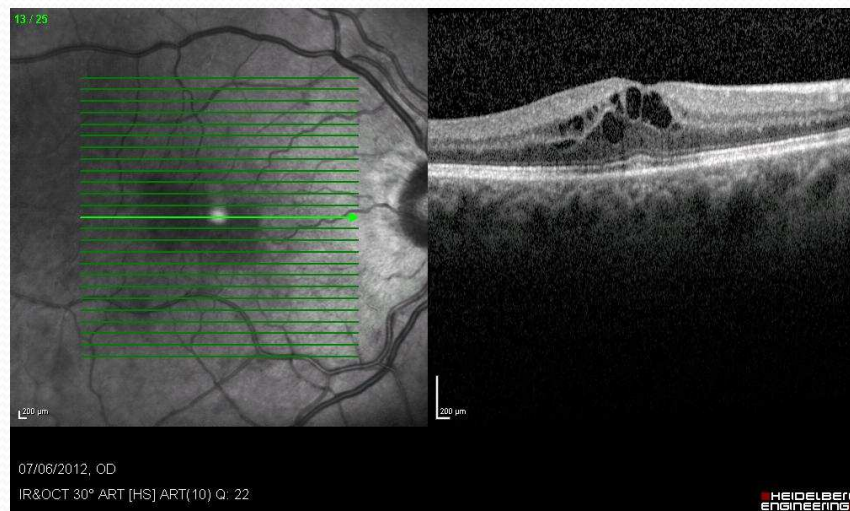
OCT June 2015



CASE 3 Mrs SF

- 68 year old Caucasian lady
- 2012: Referred by DESP
- VA RE 6/9 LE 6/9
- DR RE R₁M₁ LE R₁M₁

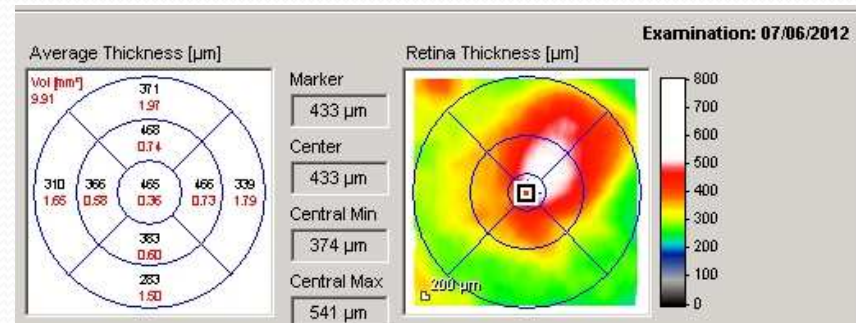
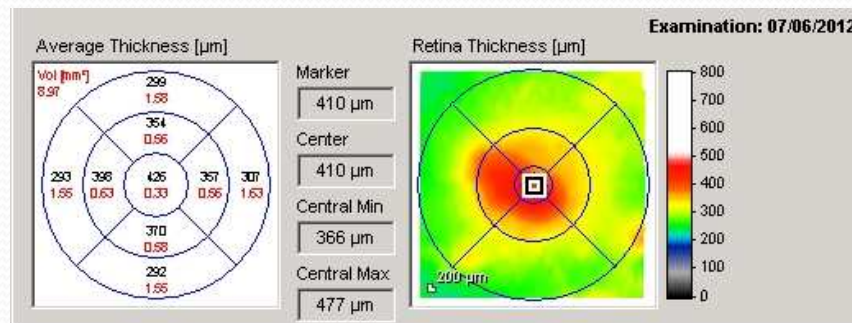
OCT JUNE 2012



OCT JUNE 2012

426 microns

465 microns





OPTIONS ?



OPTIONS

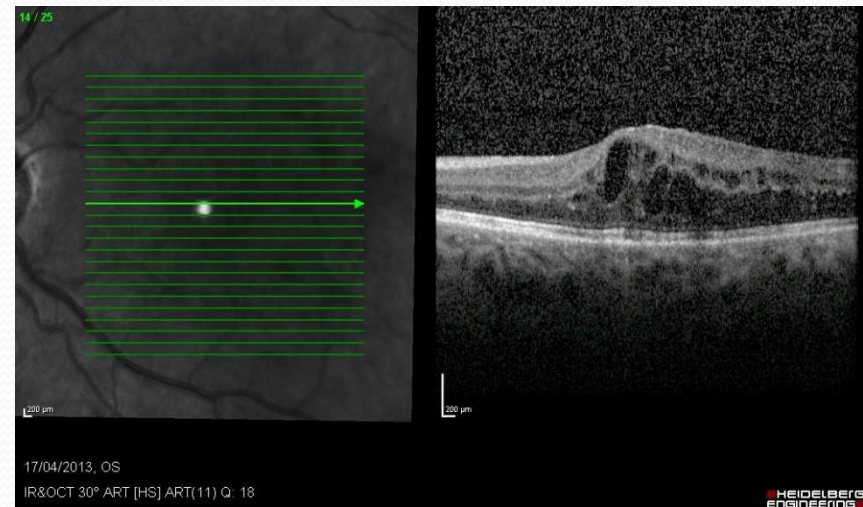
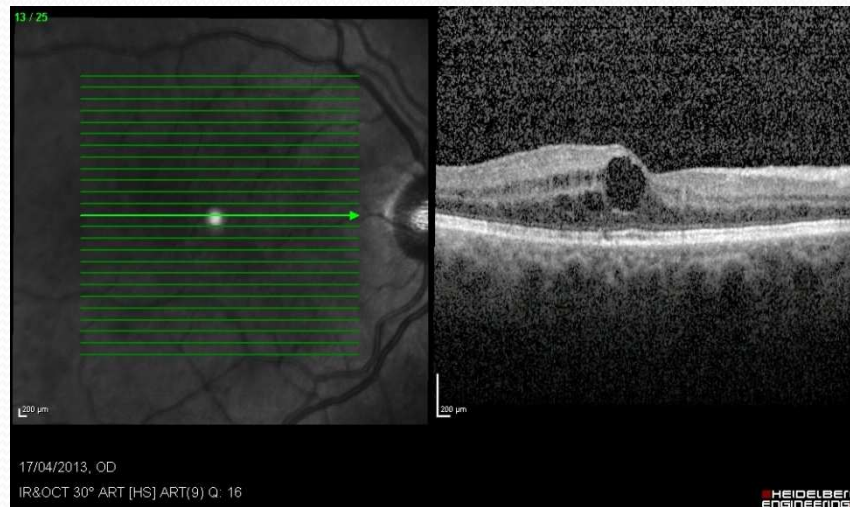
- Improve diabetic control
- Focal macular laser both eyes – June 2012

OCT April 2013 FFA ?ischaemic

470 microns

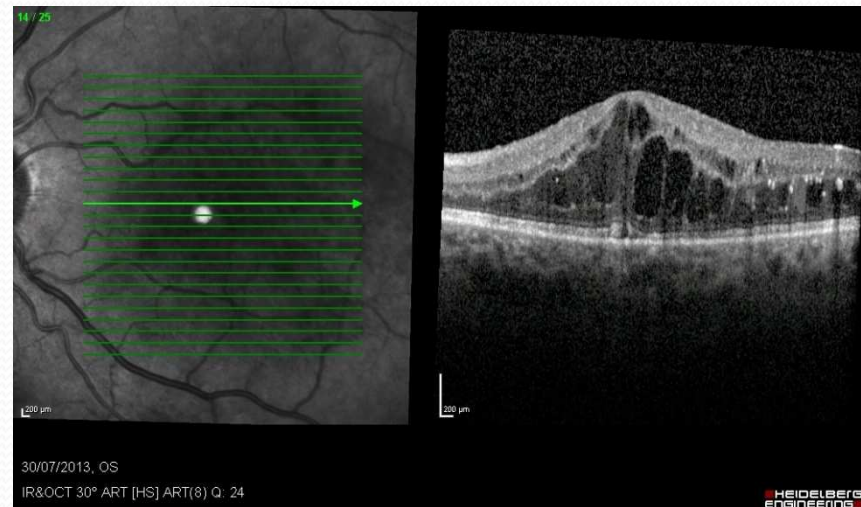
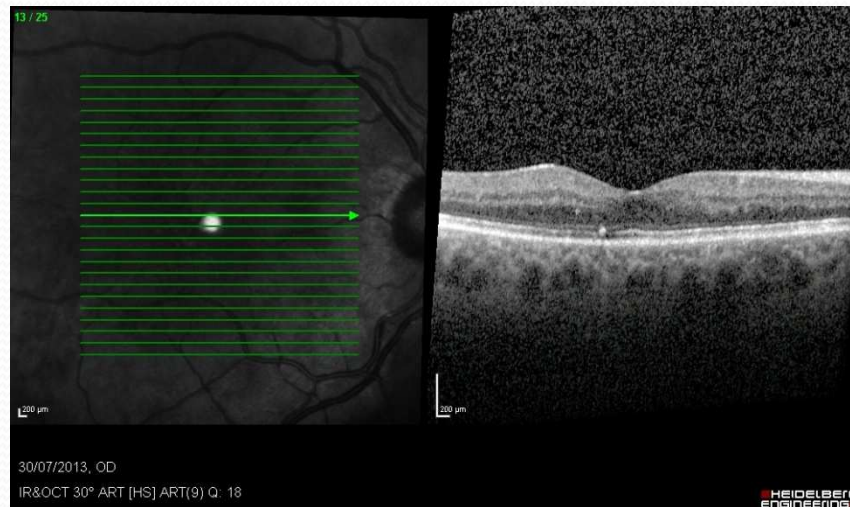
Listed for Right Lucentis

561 microns



OCT July 2013

561 microns
Listed for Left Lucentis



Outcome June 2015

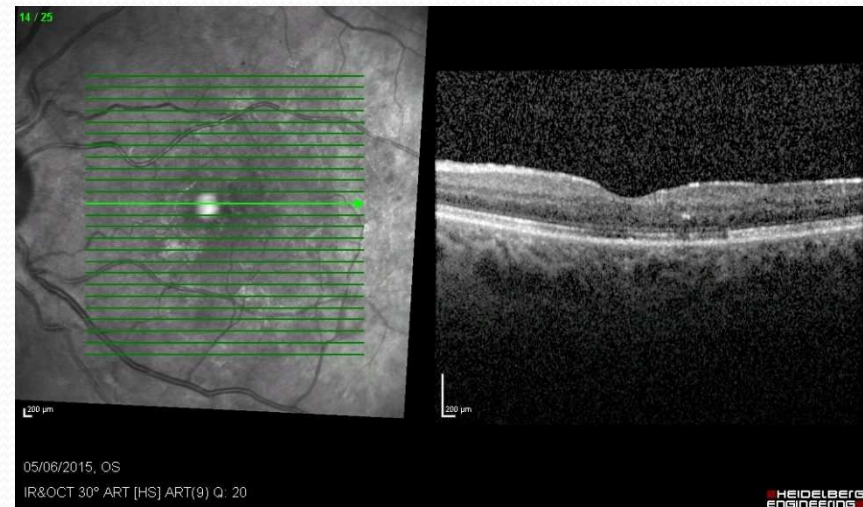
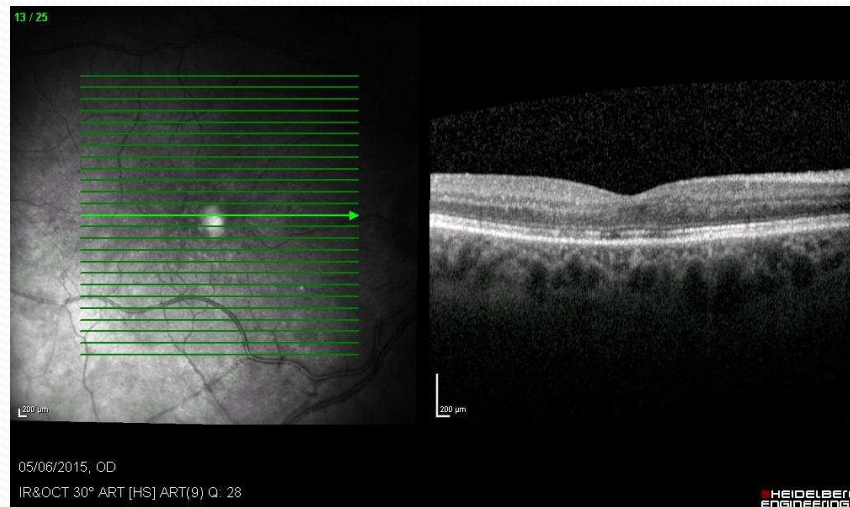
• Lucentis	13 injections	12 injections
• June 2015	VA RE 6/7.5	VA LE 6/7.5
• OCT	258 microns	258 microns

OCT June 2015

Lucentis
VA
OCT

13 injections
RE 6/7.5
258 microns

12 injections
VA LE 6/7.5
258 microns



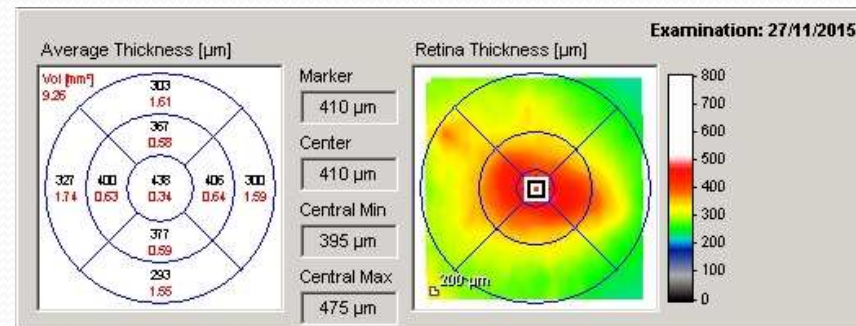
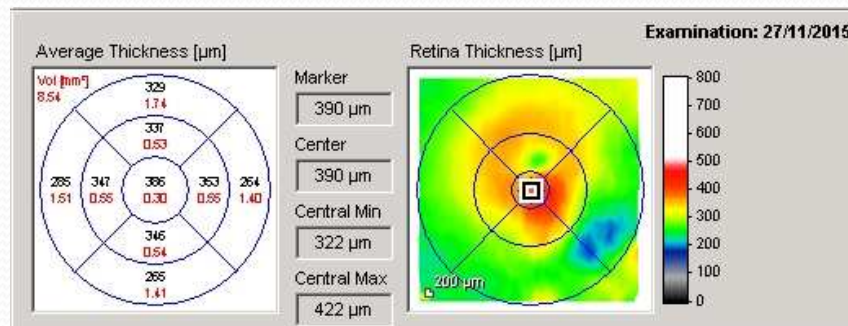
Case 4 Mr RD

- 69 year old Caucasian male
- Referred by DESP
- Driver
- DR: RE ungradeable LE R₁ M₁
- VA RE 6/36 UA VA LE 6/18 UA (6/12ph)
- Bilateral cataracts

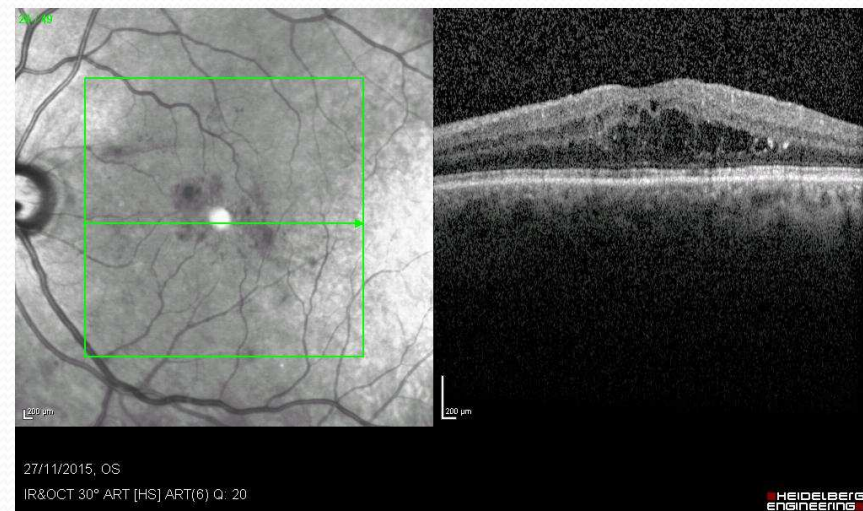
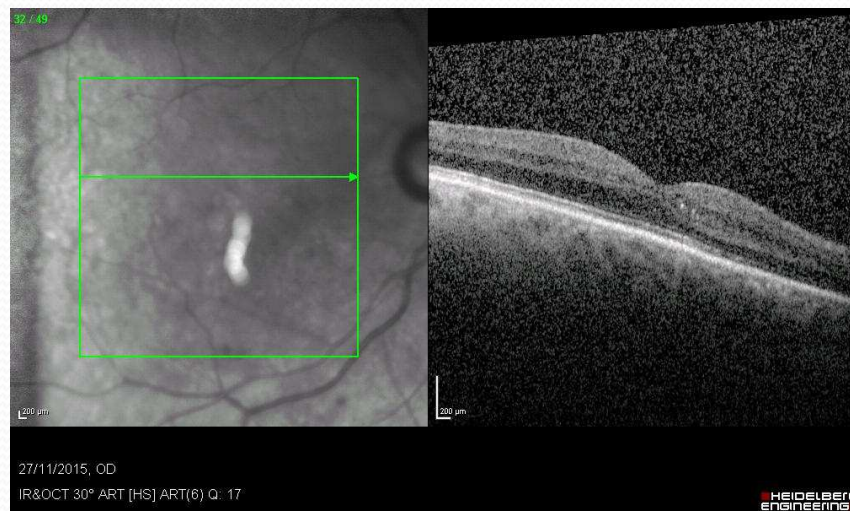
OCT November 2015

386 microns

438 microns



OCT November 2015



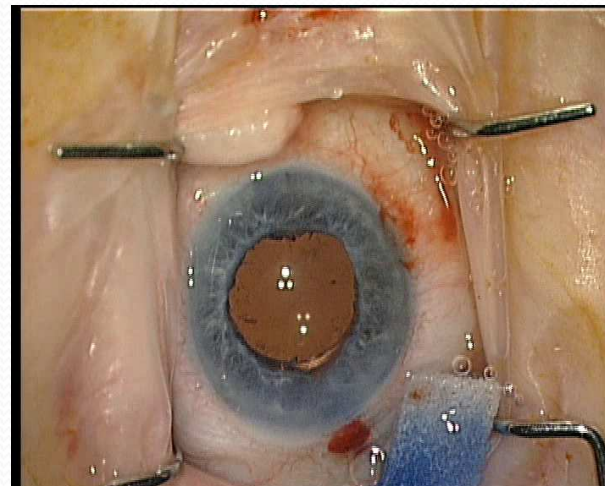
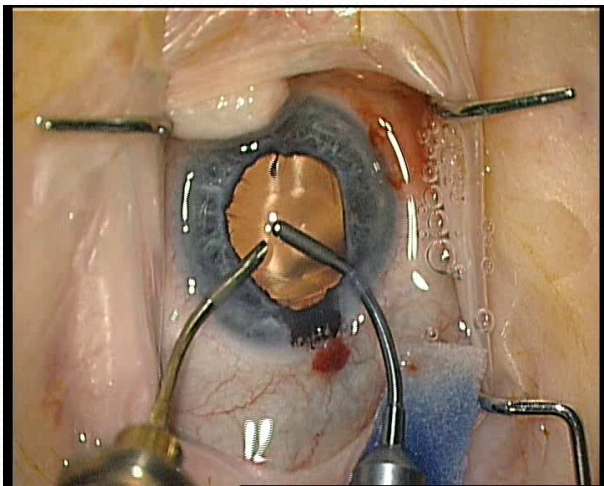
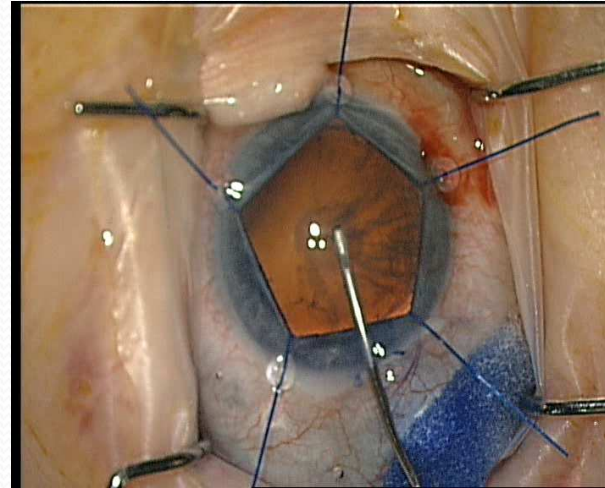
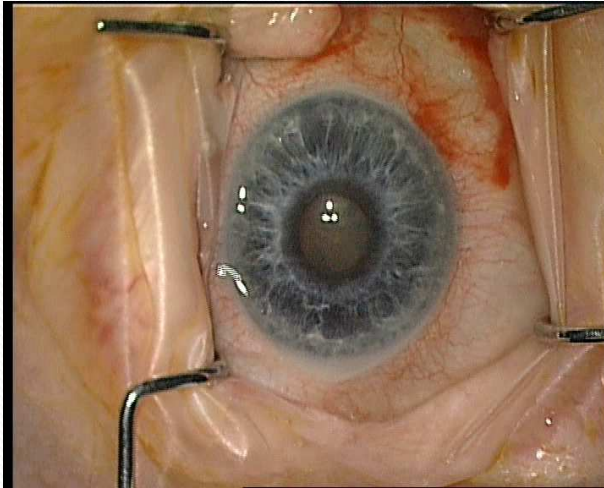


OPTIONS ?

OPTIONS

- Driver
- Advised not to drive! (6/36, 6/18)
- Listed for right Cataract surgery + IOL + IVTA
- Listed for Left Eylea

Cataract surgery in diabetics



Pseudophakic DMO

- First line

Topical NSAIDs

Bromfenac (Yellox)

Flurbiprofen (Ocufen)

Ketoralac (Acular)

Nepafenac (Nevanac)

Topical steroids

?Diamox

- Second line

Orbital Floor Depomedrone

Triamcinolone (subconj, subtenons, IVT)

Ozurdex IVT

Case 5 Mr GG

- 68 year old Italian gentleman
- Type 2 diabetes; now on Insulin
- 2005: **Focal Macular laser**

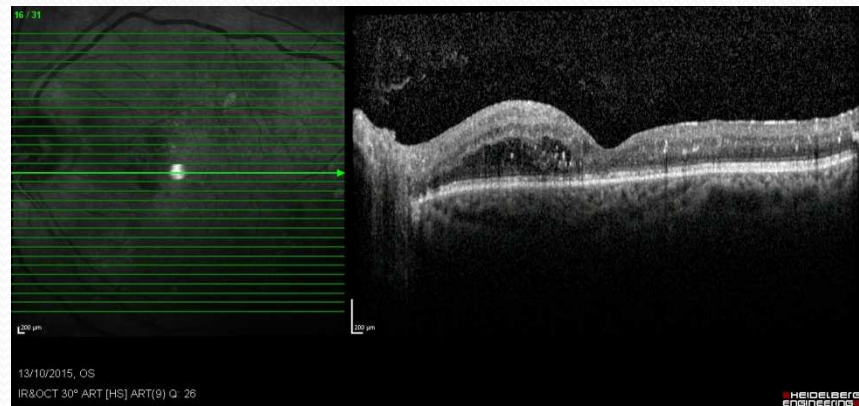
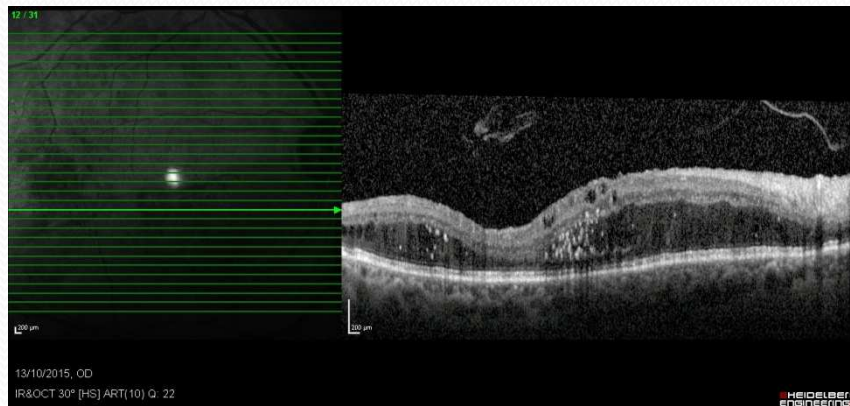
09/2005	09/2005
02/2007	02/2006
07/2007	12/2007
03/2008	03/2008
04/2011	09/2011
09/2011	
- 2013 **IVT Lucentis**

7 injections	5 injections
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October 2015

VA 6/15
CMT 304

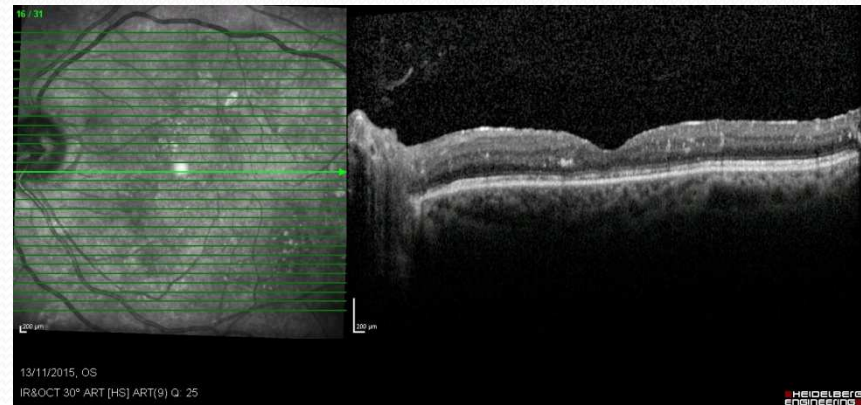
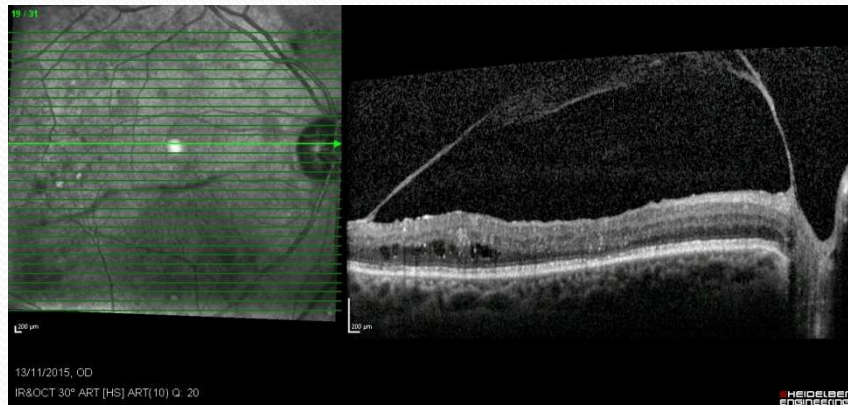
VA 6/30
CMT 237




November 2015

VA 6/12
CMT 268

VA 6/24
CMT 258



- 
- Oct 2015 IOPs 18/18
Triamcinolone – steroid challenge
 - 1 week IOPs 11/13
 - Nov 2015 IOPs 21/15
 - Dec 2015 ?

DMO - Where are we now

- Lucentis and Eylea approved
- Eylea 34% more 15 letter gain
- Combined laser and anti-VEGF has a role

Pseudophakic:

- Ozurdex 2nd line < 18 months
- Iluvien 2nd line > 18 months

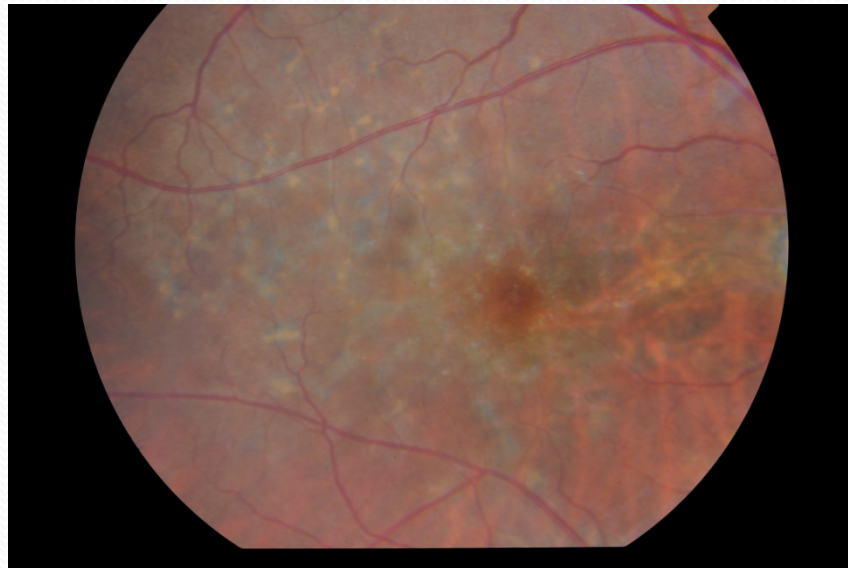


Cataract surgery: Aim for optimal control of DMO

Case 6 Mrs AS

- 72 year old Caucasian lady
- Type 2 diabetes
- 1994: VA RE 6/6; VA LE 6/6
- 1996: Optometrist referral (53 years)
RE: +0.25/-0.50 x 90 6/9 +2.25 Add
LE: +0.75/-0.75 x 90 6/18 +2.25 Add
Discharged
- 1999: Left phaco, no DR, discharged
- 2014: Referred for right cataract, macular exudate
- 2015: Right phaco (Aug)

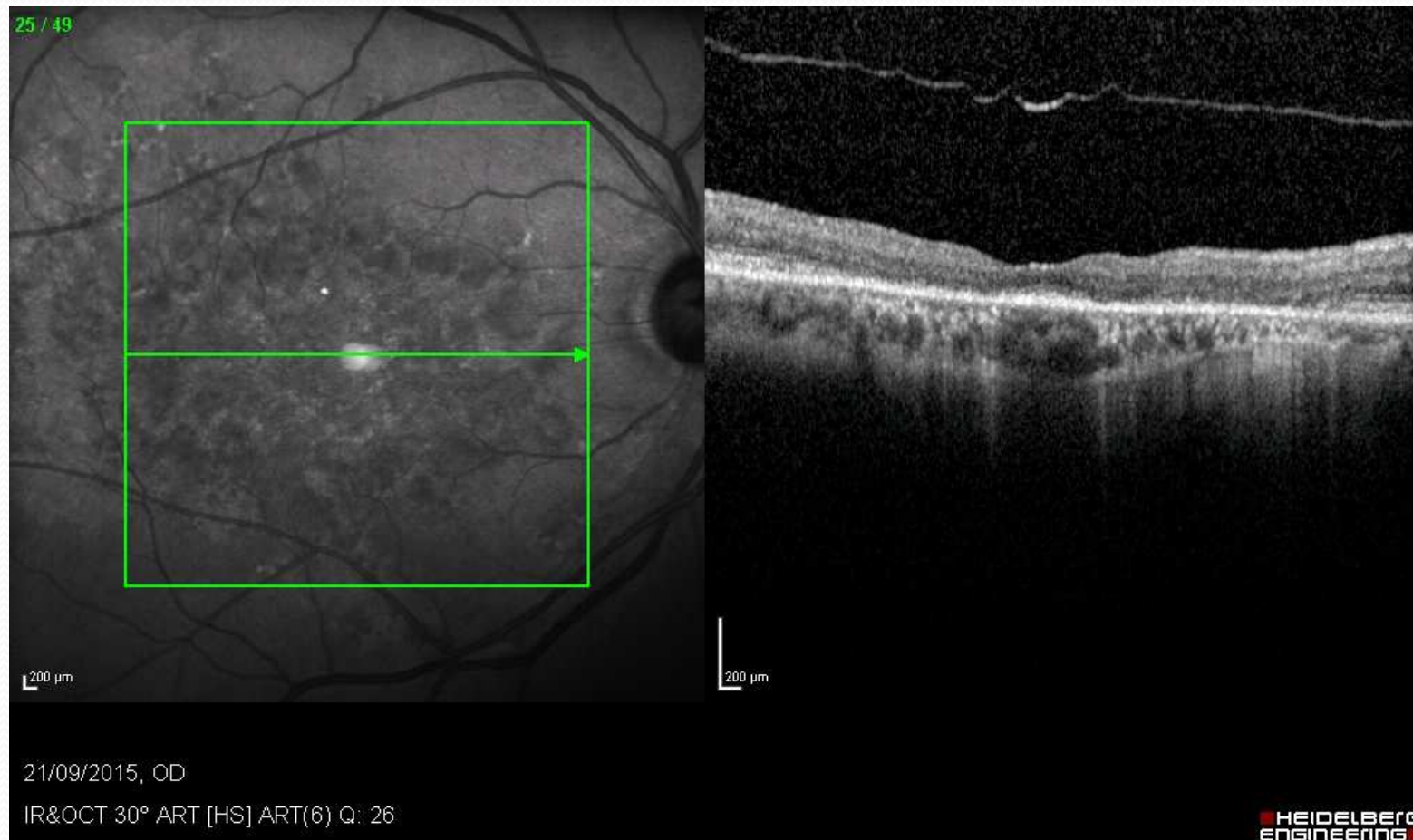
Colour September 2015



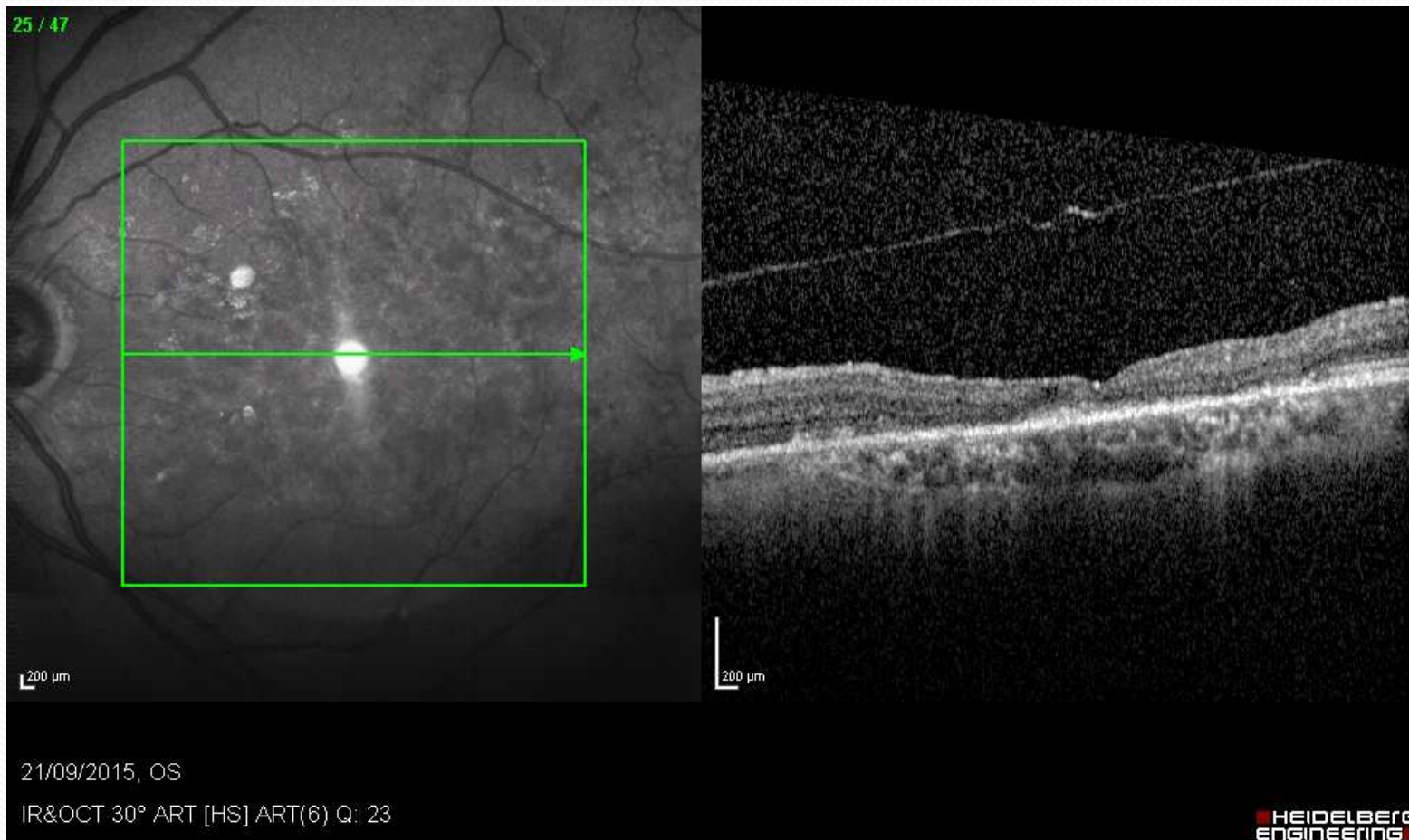


Options?

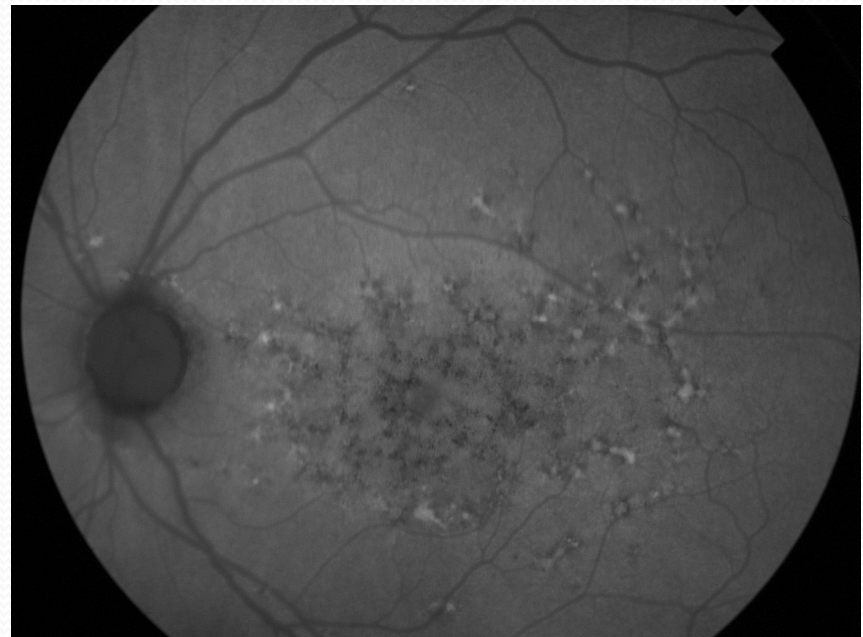
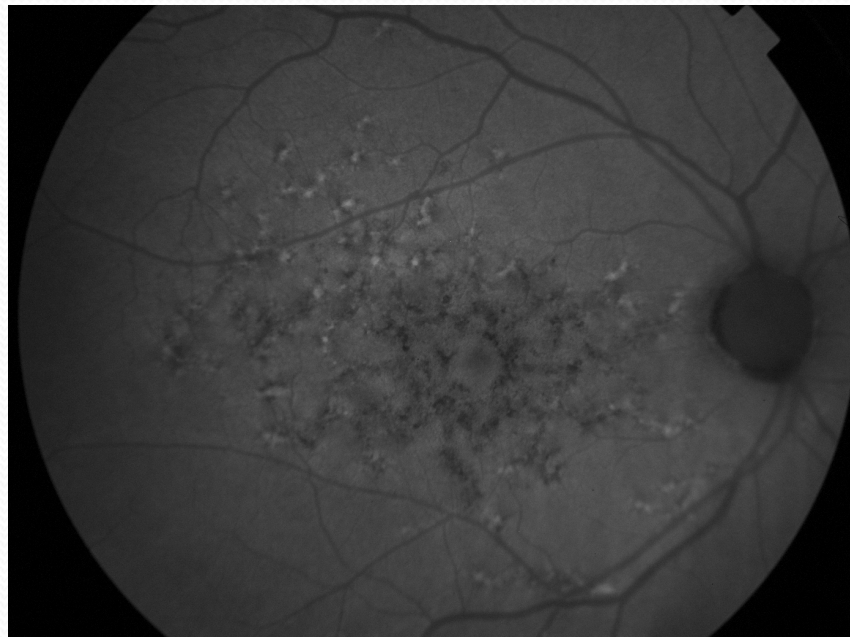
OCT RE September 2015




OCT LE September 2015



FAF September 2015



- 
- Not Diabetic Retinopathy!
 - Undiagnosed Stargardts's Dystrophy/ABCA4
 - Referred MEH
 - Diagnosis confirmed by EDD (10/11/15)



UVEITIS SERVICE

- **UVEITIS CLINIC**

Monday 1.30 – 5.00 pm

- NHS secretary

Sally Bargery:

Email: sally.bargery@ldh.nhs.uk

Phone: 01582 497329

- Private secretary

Angela Sborgia

Email: angela@ranjitsandhu.co.uk

Phone: 0800 042 0258

ACUTE EYE CLINIC

- **Between 9.00 am - 5 pm**

Immediate: 01582 718320

Non-urgent: 01582 718418

Bleep - Acute Eye Clinic Nurse Practitioner

- **After 5 pm**

L&D switchboard

Ophthalmologist on call





Thank you for listening!

www.ranjitsandhu.co.uk

EMAIL: binnie@ranjitsandhu.co.uk