ILUVIEN IN DIABETIC MACULAR ODEMA

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bars conference 2104

Declaration of interest

- I have sat on Advisory boards for Novartis and Bayer
- Involved in Novartis sponsored clinical trials
- Involved in Allergan sponsored clinical trials
- Sponsored by Novartis and Bayer and Alimera at various clinical meetings

What does DR screening actually mean for the patient?? In the HES .Why is it so important?

- Strict criteria laid down by the National Screening Service means patients have to be seen and treated within a certain time period

- monitored and strictly adhered to
- Eg. new Proliferative disease: seen and receiving first treatment (laser) in HES within 20 working days
- Routine referrals within 13 weeks

- **Earlier diagnosis and treatment reduces visual loss in diabetic retinopathy**

Prevalence – the numbers. UK

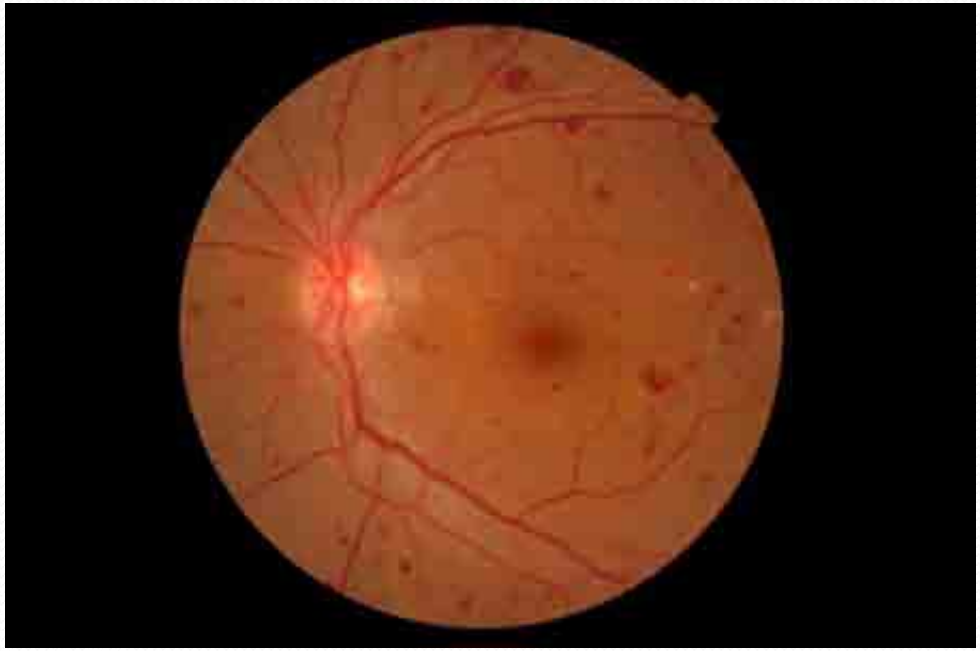
- **REMEMBER.** DR is still the major cause of blindness in the working population !!
- There are over 3.2 million people who have been diagnosed with diabetes in the UK

- Prevalence is 6% and rising

- HES at the QE???
- Clinic visits in 12 months - 48,000
- 17, 000 appts for diabetic eye disease
- 182 active patients under MDT having multiple injections for DMO

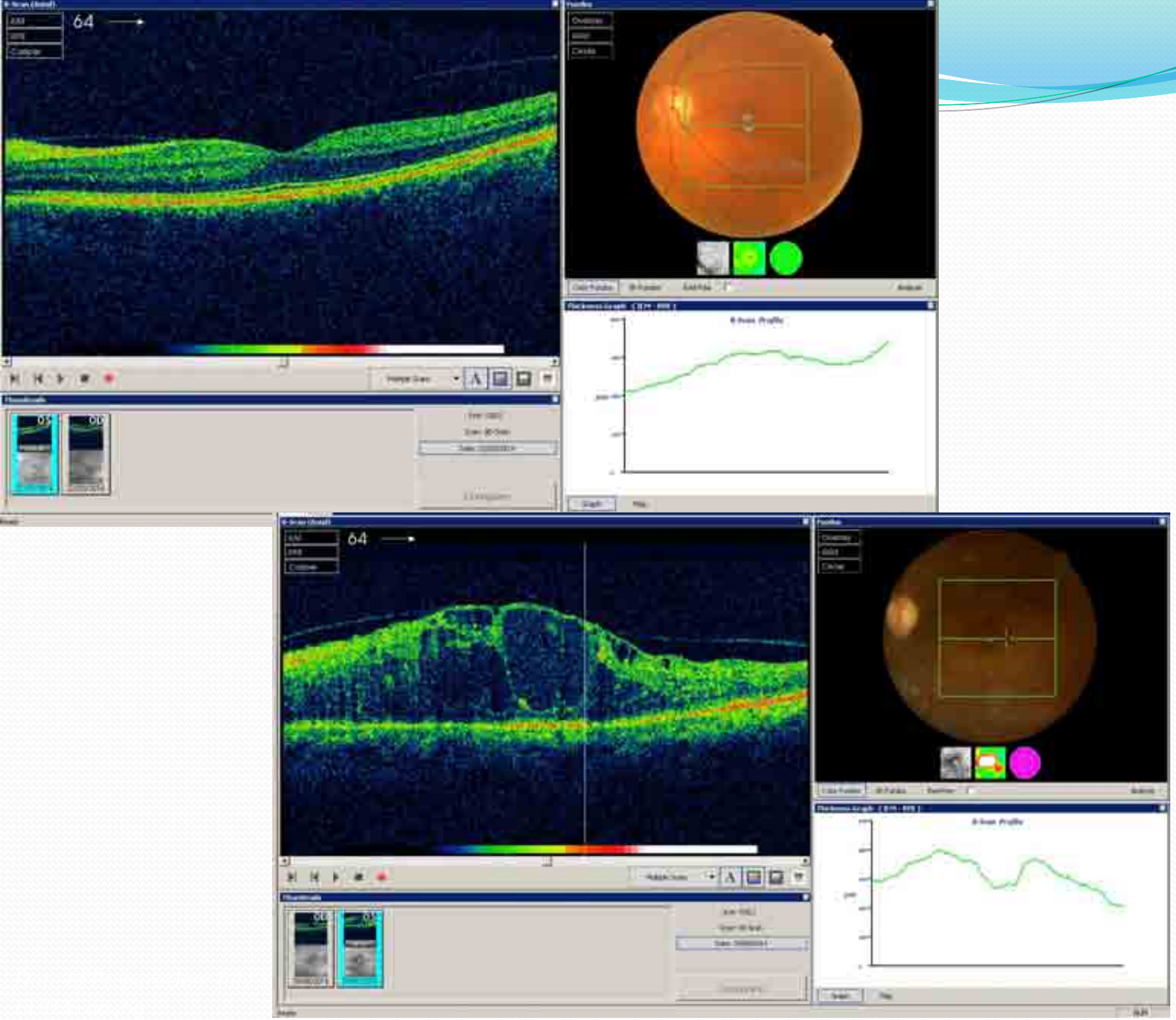
PROLIFERATIVE DR

- Treatment with pan retinal laser reduces the risk of visual loss by more than 50%
- Still the mainstay of treatment
- Advances in laser technology has reduced incidence of nyctalopia and scarring and reduced visual field
- New mulitspot lasers reduce patient discomfort, reduce application time and increase compliance



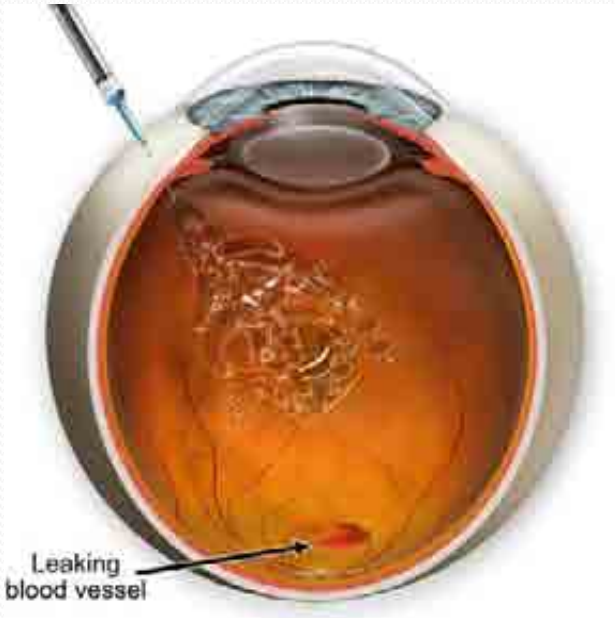
New Treatments – exciting times

- What's changed??
- Treatments for Diabetic Macular Oedema
- **OCT.** (Optical coherence tomography) has allowed us to see pathology in the macula with much greater accuracy
- undiagnosed DMO or inaccurate assessment of the severity of DMO was often a cause of visual loss



Everything works to a certain degree!!

- What are we trying to achieve??
- improvement in vision that lasts
- decrease in central retinal thickness on the OCT scans
- Avoid sequlae
- With a minimum of intervention!
- Lucentis - NICE
- Avastin
- Triamcinolone
- Iluvien -NICE



The Diabetic Retinopathy Clinical Research Network

Randomized trial evaluating
* ranibizumab plus prompt or deferred laser
* or triamcinolone plus prompt laser
* laser alone

for diabetic macular oedema

Ophthalmology 2010;117:1064–77
Ophthalmology 2011;118:609–14
Ophthalmology **2012;119:2312–8**

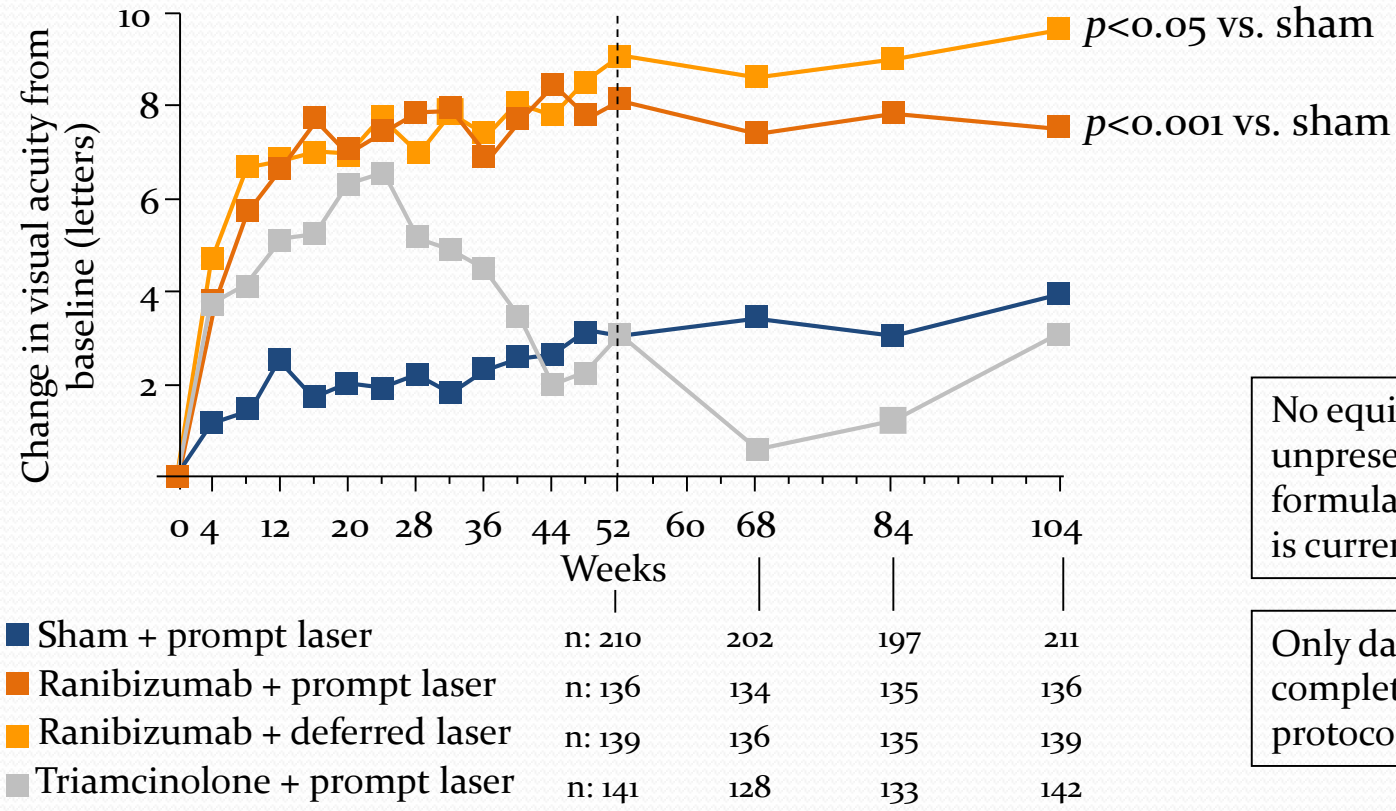
No equivalent to the unpreserved triamcinolone formulation used in this study is currently available in the UK. Triamcinolone available in the UK is contraindicated for use in the eye

Prescribing information appears at the end of this presentation

Key results:

mean change in visual acuity from baseline

Ranibizumab treatment, regardless of timing of laser therapy, resulted in significantly greater improvement in visual acuity than sham + laser

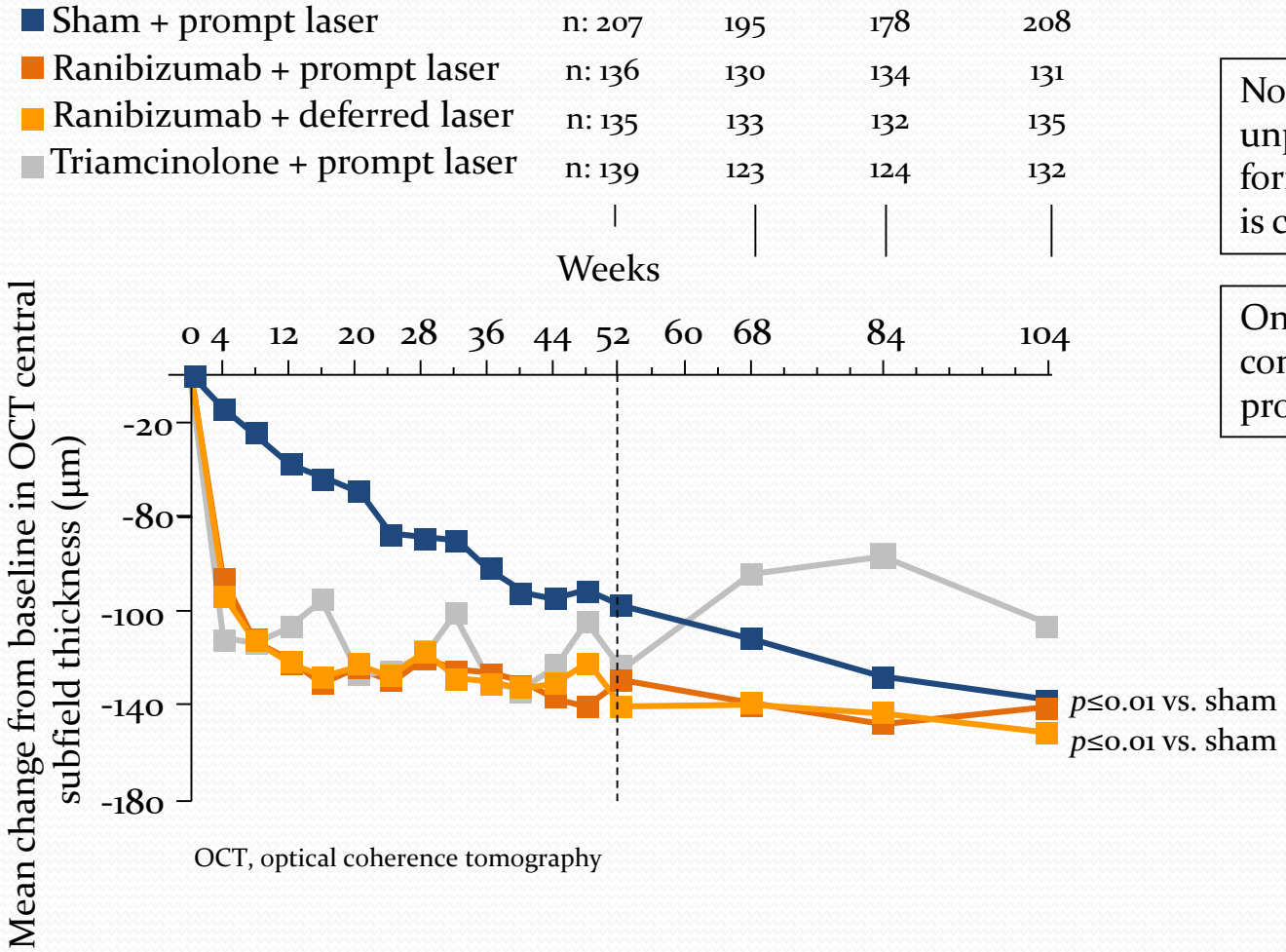


No equivalent to the unpreserved triamcinolone formulation used in this study is currently available in the UK

Only data from those who completed year 2 before the protocol change are included

Elman et al. *Ophthalmology* 2011;118:609–14

Key results: retinal thickening



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Triamcinolone AND Iluvien

- why steroids??

- Macular oedema has a multifactorial pathogenesis of which inflammation is a recognized cause
- Benefits in macular oedema are well documented
- Especially refractory diabetic macular oedema that does not respond to anti-vegfs
- Reduce VEGF expression and vascular permeability and suppress inflammation

- Multiple series show beneficial effect.
- resulted in improvement in vision at 3 -6 months but not maintained
- Why? Cataract formation
- Rise in IOP at 3 months
- NICE approved Iluvien use in pseudophakic eyes

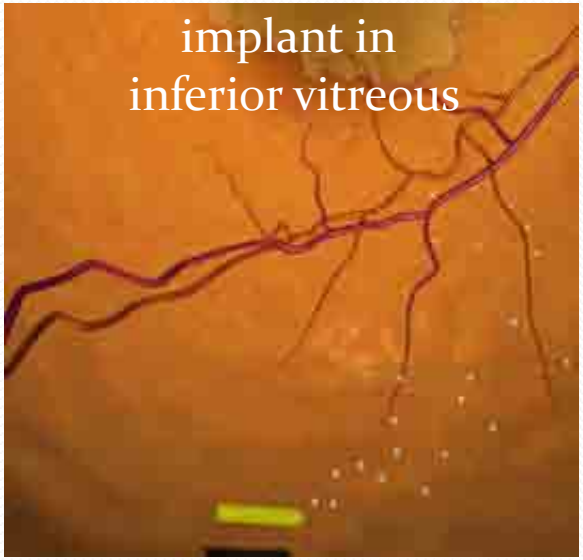
ILUVIEN for DMO

ILUVIEN 190 micrograms fluocinolone acetonide (FAc) intravitreal implant in applicator.

Sub-microgram sustained delivery of 0.2 µg/d FAc for up to 36 months

3.5 mm × 0.37 mm non-bioerodable micro implant.

25-gauge injector creates self-sealing wound.



NICE guidance

- **CE technology appraisals [TA301]** Published date: November 2013

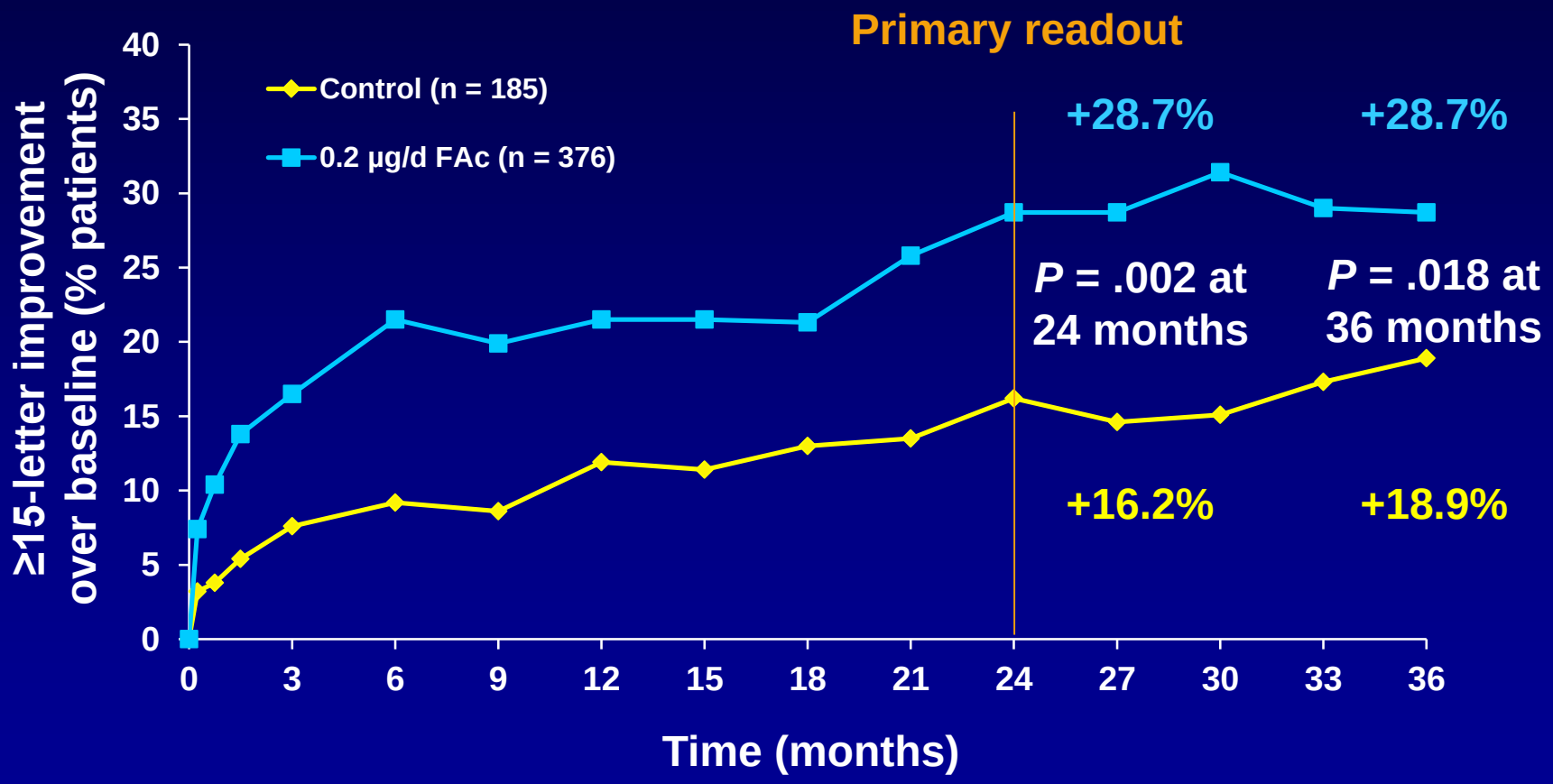
- Fluocinolone acetonide intravitreal implants are recommended as a possible treatment for people with chronic diabetic macular oedema who have an artificial lens in their eye if:
- the implant is used in the eye with the artificial lens **and**
- their diabetic macular oedema has not got better with other treatments.

ILUVIEN

1. ILUVIEN is a very long acting treatment for DMO.
2. ILUVIEN is used to resolve oedema.
3. ILUVIEN improves visual acuity.
4. Efficacy is greatest in chronic DMO patients.
5. Secondary IOP rise can be managed with good visual outcomes.
6. Cataract removal can be managed with good visual outcomes.

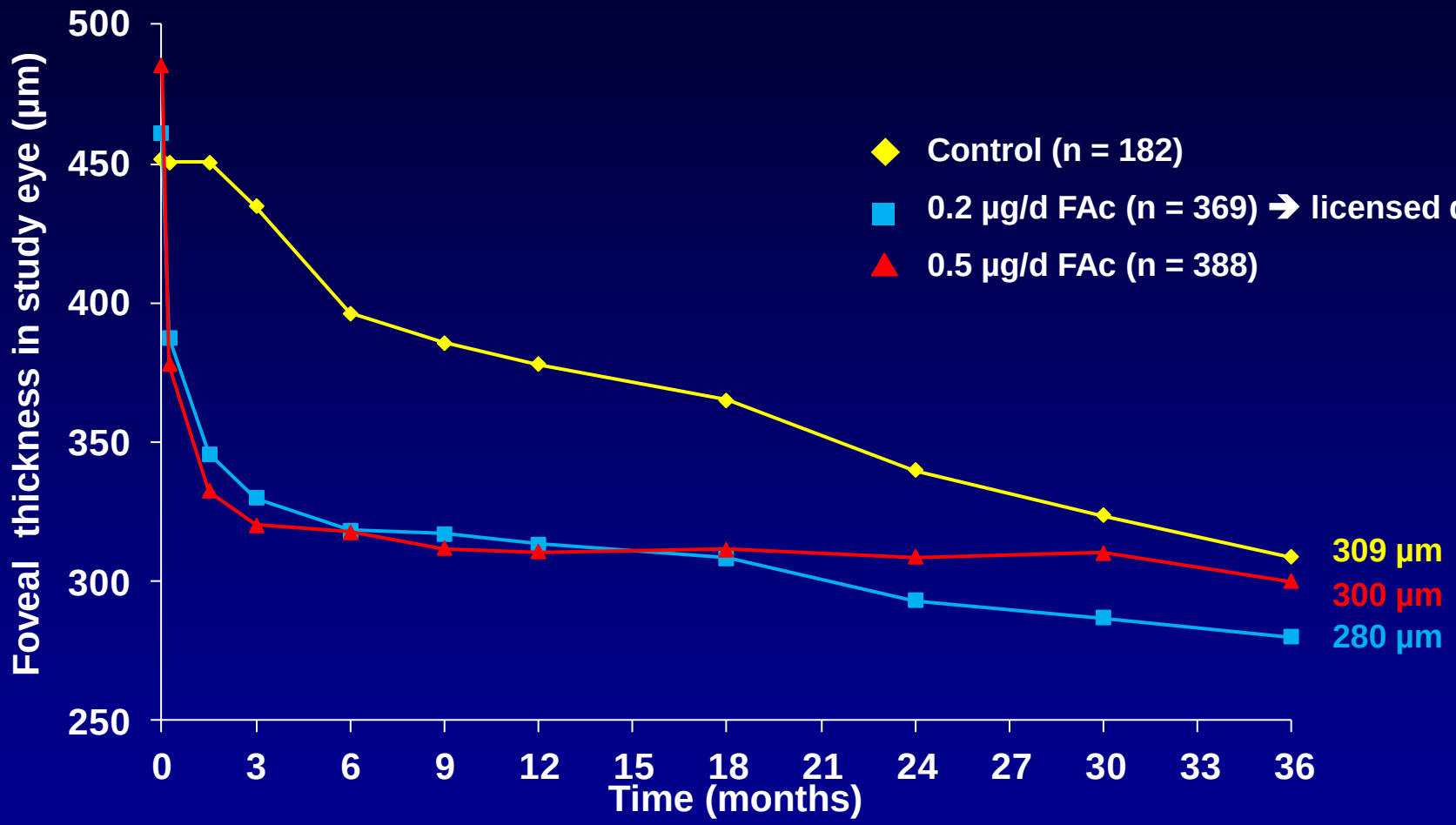
ILUVIEN improves visual acuity

Full population



ILUVIEN SPC. http://www.medicines.org.uk/emc/medicine/27636.

Effective reduction in retinal thickness



A rapid reduction was seen in those treated with lower dose FAc

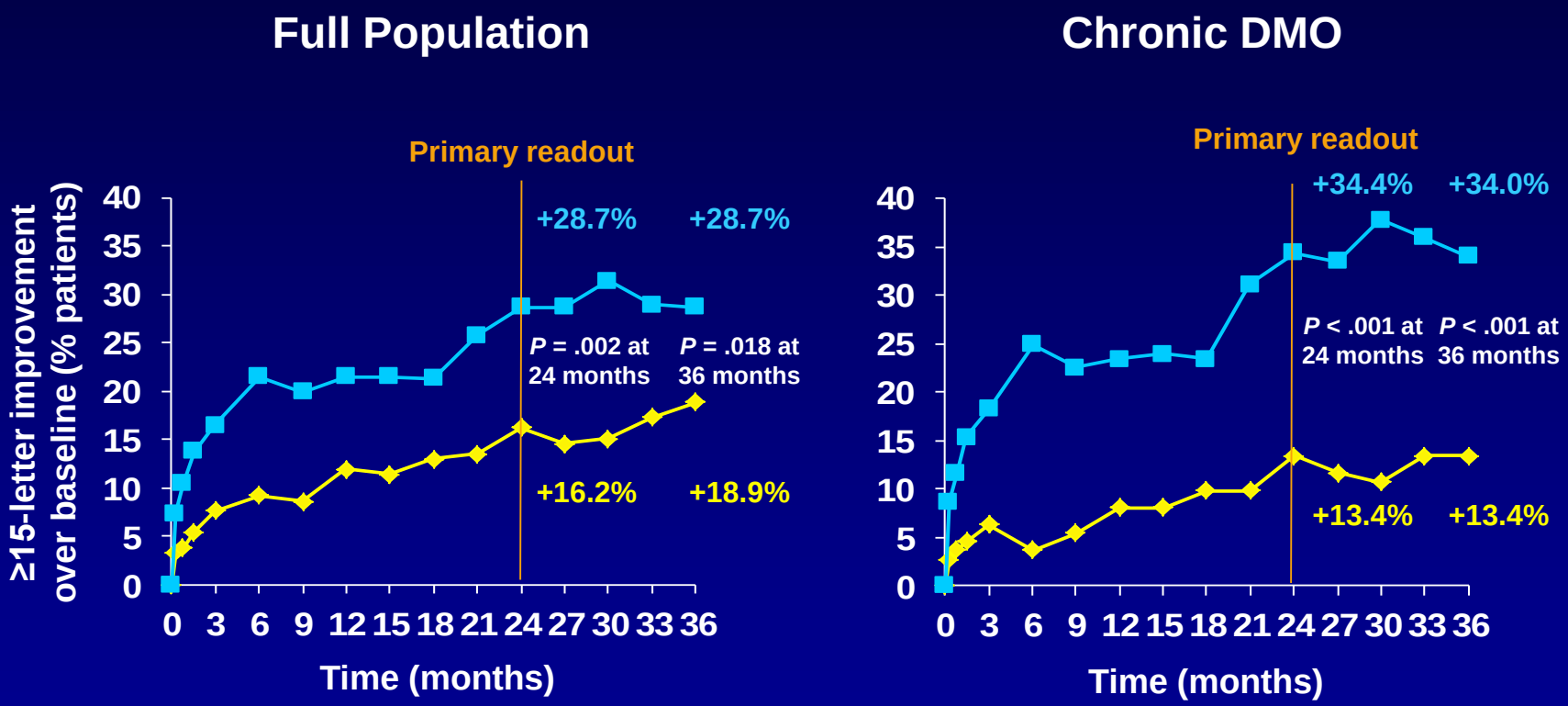
Date of Preparation: July 2014
EUILV-0048g

Campochiaro PA, et al. Ophthalmology. 2012;119:2125-2132.

Subgroup Analysis

- Outcomes were assessed in patients with DMO at baseline with duration of DMO < 3 years versus duration greater > 3 years
- The percentage of patients who gained> 15 letter score was greater in the chronic DMO than short duration years DMO (< 3 years) compared to sham
- **Rescue treatments**: focal / grid laser treatments was the standard of care for DMO during the study
- Significantly higher percentage of patients in the sham group received focal grid laser treatment
- During the trial other intravitreal injections were not allowed as rescue treatments

Efficacy is greatest in chronic DMO patients



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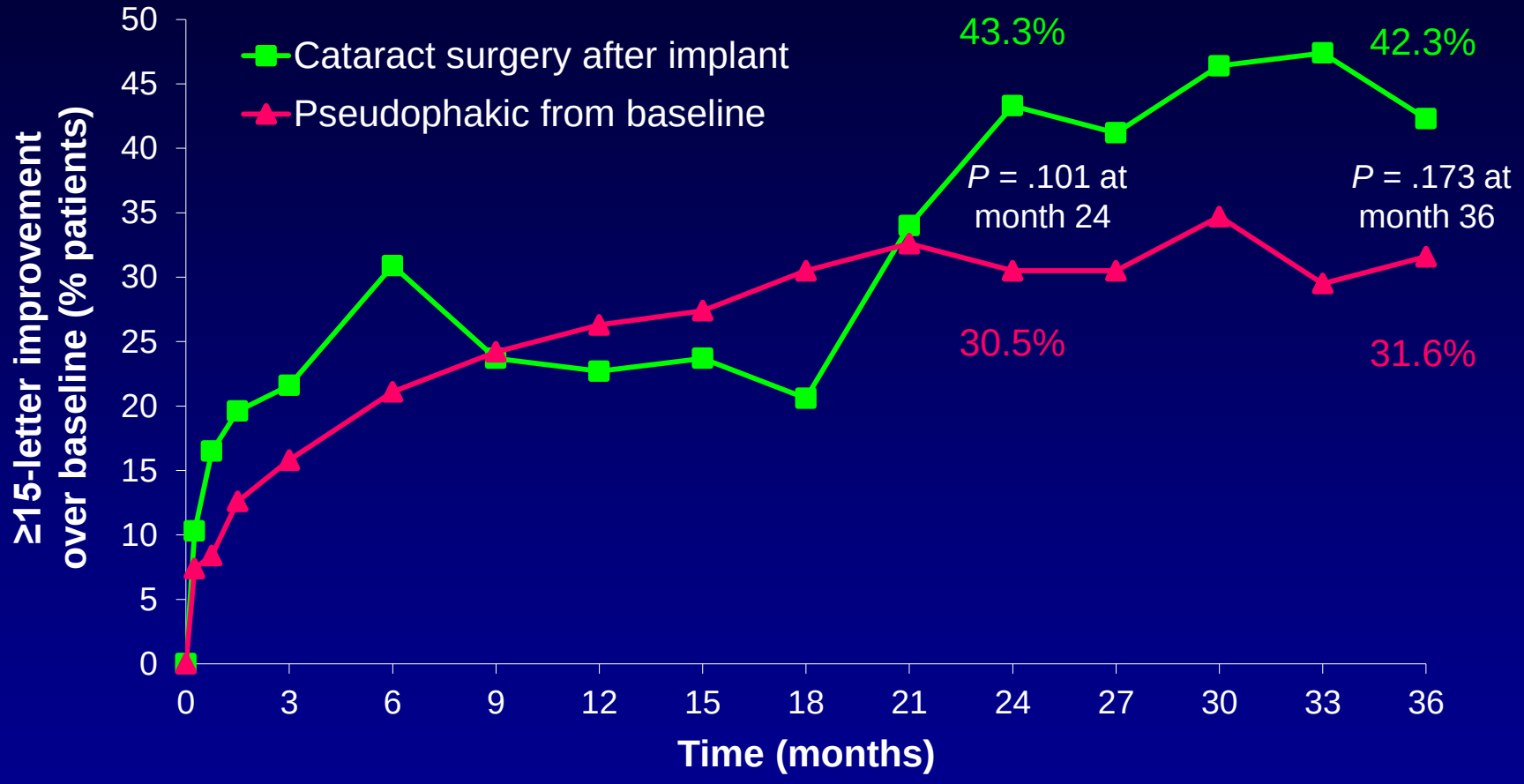
ADVERSE EVENTS

- Most common was cataract development
- **42.7 % in the treated group Vs 9.7% in the sham group**
- Median time cataract was reported as an adverse event was 12 months and median time for cataract surgery was 18 months
- Development of cataracts coincided with diminished vision improvements during months 6-18
- Cataract surgery did not diminish post-surgery or long-term best corrected visual acuity gains

6. Cataract removal can be managed with good visual outcomes



Post-hoc analysis revealed that chronic DMO patients had good visual outcomes irrespective of lens status

Data on File #28. Alimera Sciences.

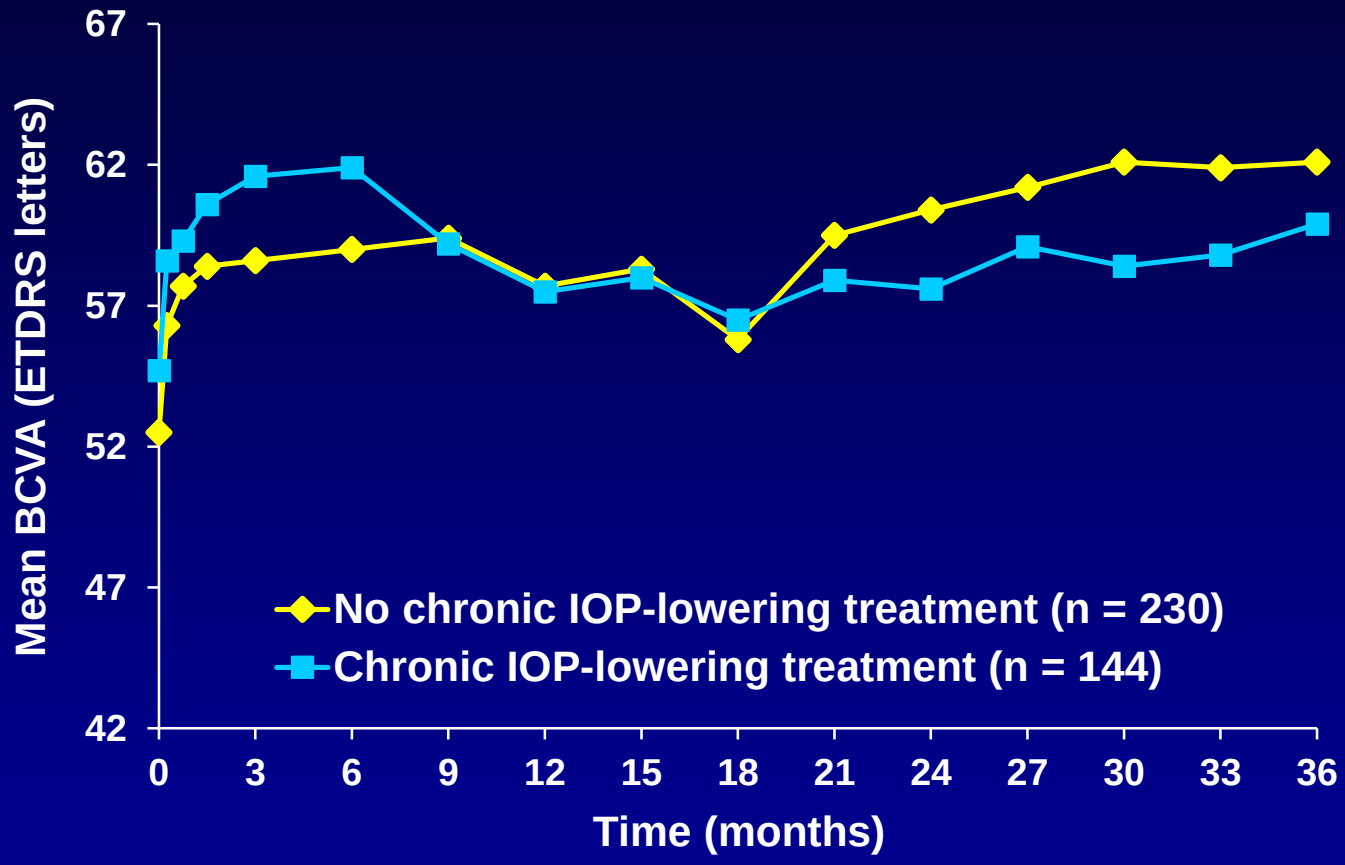
Intraocular pressure related events

- (*Patients were excluded from the study if they had diagnosed glaucoma, IOP > 21 or where on pressure lowering drops)*

- 38% patients treated with single ILUVIEN implant required IOP lowering medication
- Of the patients treated with IOP-lowering medications - 48% required only a single medication
- 18.4% of patients given ILUVIEN had an IOP >30 mmHg
- 70% of IOP elevation occurred in the first year

- 1.3% required laser trabeculoplasty to address the elevated IOP
- 4.8% required incisional surgery to address elevated IOP
- Raised IOP did not adversely affect visual acuity outcomes

5. Secondary IOP rise can be managed with good visual outcomes



IOP-lowering medication status did not affect mean BCVA

Chronic defined as IOP medication taken for more than 28 days.

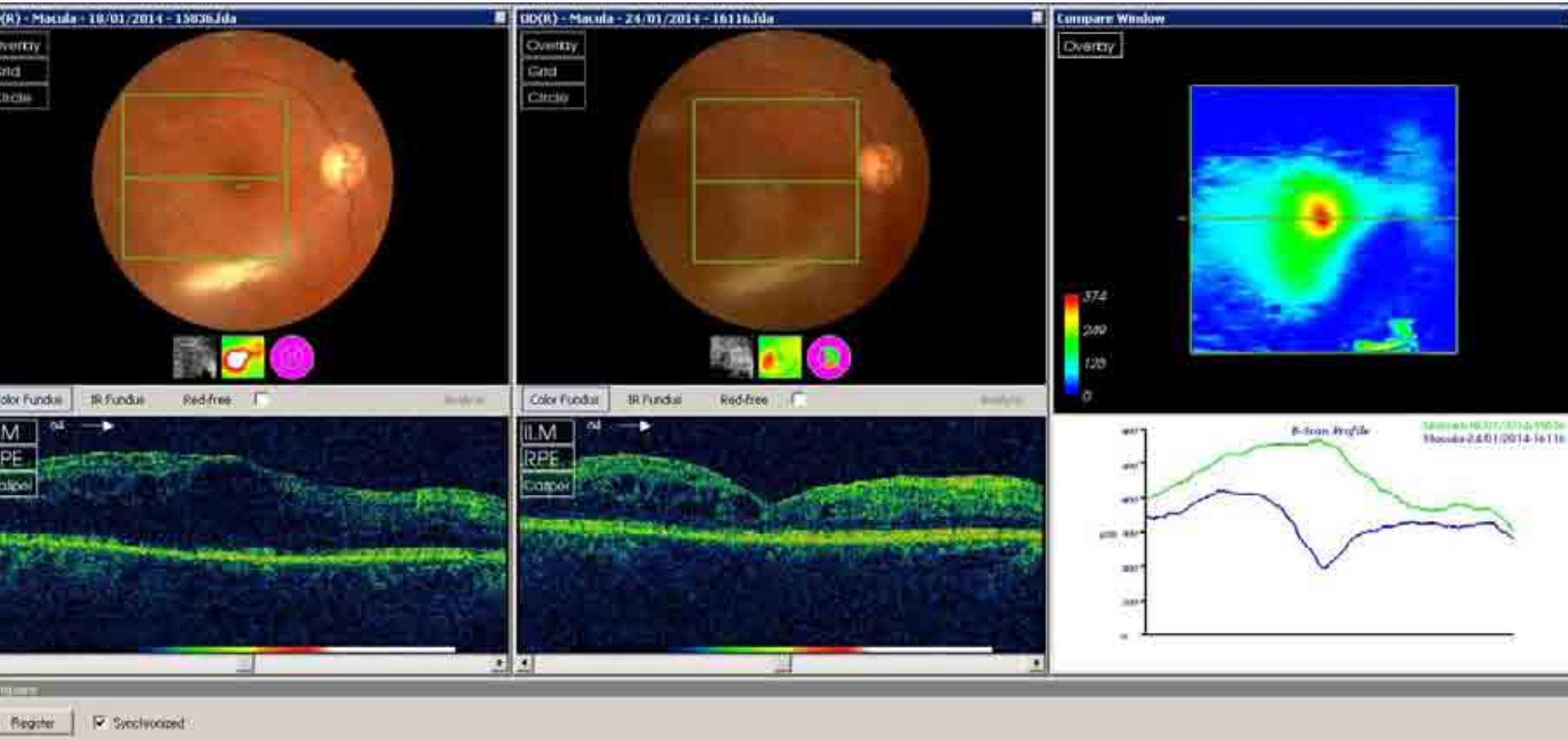
Data on File #41. Alimera Sciences.

Date of Preparation: July 2014
EUILV-0048g

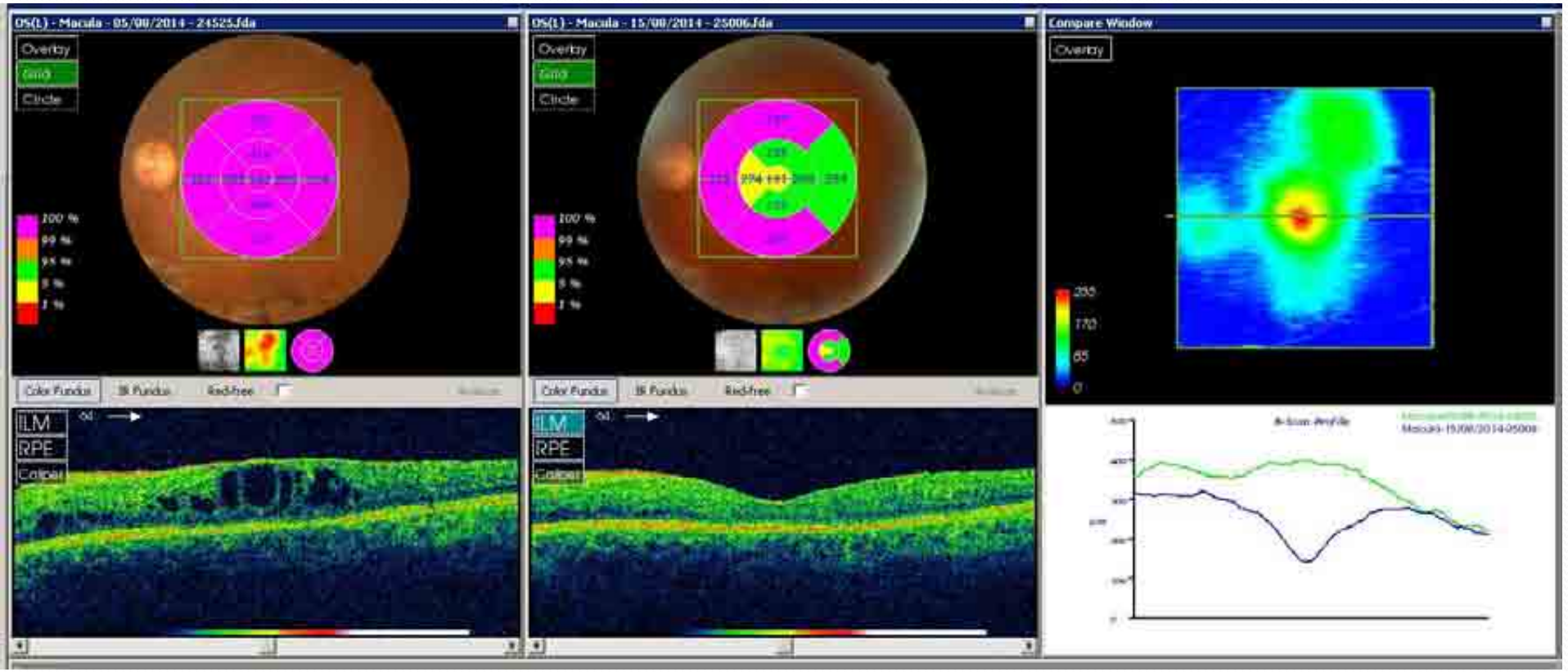
Personal experience

- QE – 15 Iluvien injections
- database of possible patients kept for 6 months before NICE approval
- several of these patients had responded to Triamcinolone before
- Protocol.
- Va and OCT on day of injection
- Then one week, 6 weeks, 3 months , 6 months
- No unmanageable rise in IOP was documented

RN. Type 1. 38 years, right eye: 6/18 > 6/12 – previous response to several injections of Triamcinolone but no response to anti Vegfs



RN, left eye – 6/60 > 6/36 Had been on Timolol after triamcinolone but not on drops at the moment,
IOP 21, 21

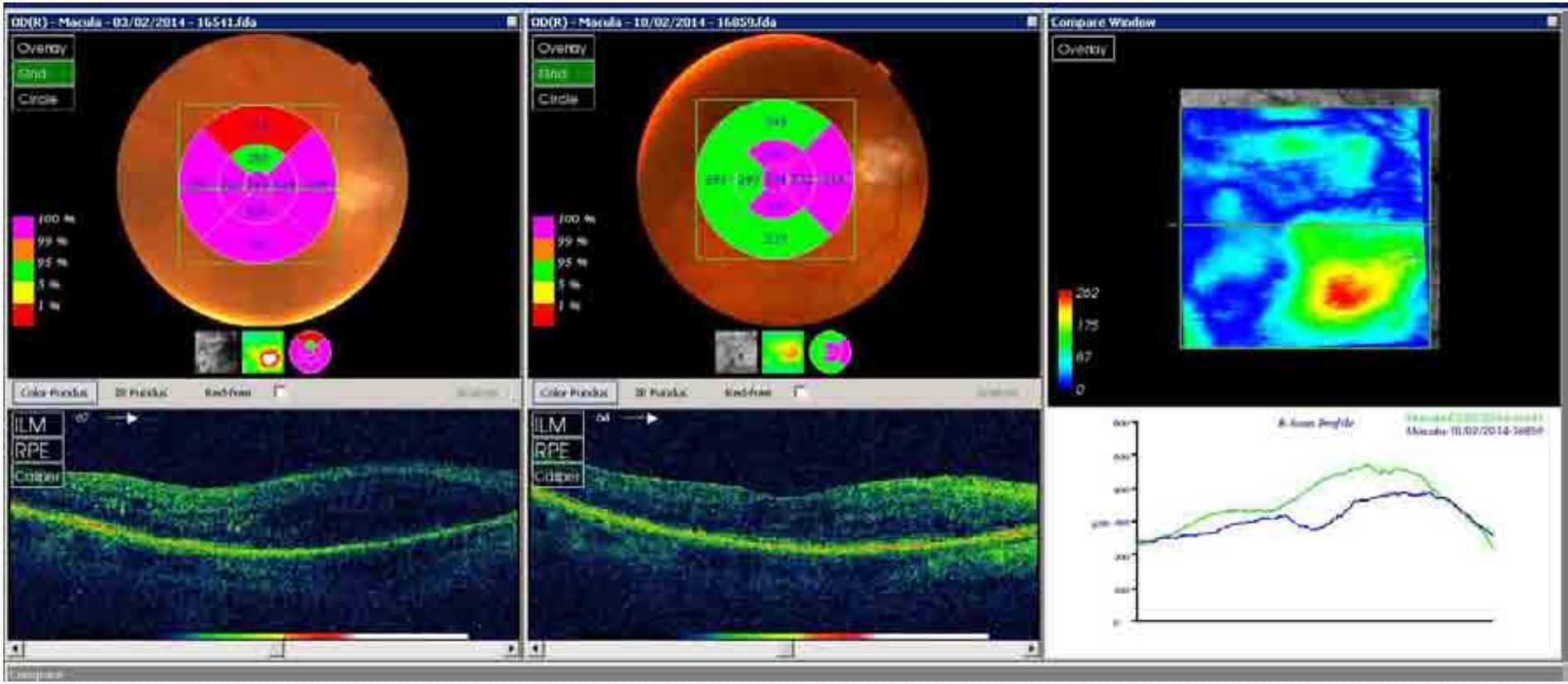


BP – type 2 on insulin. 82 years

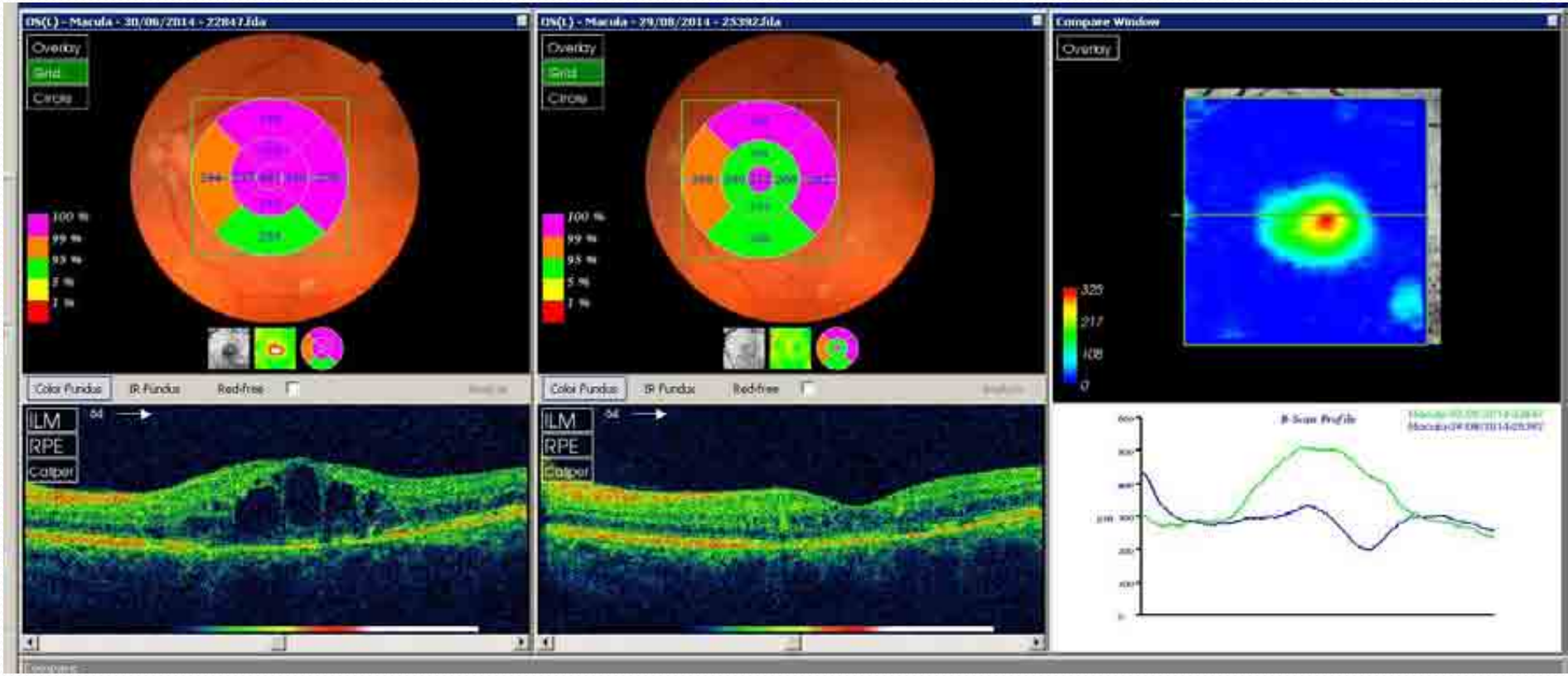
Va 6/24 to 6/18

3 avastin before with no response, no IOP treatment needed

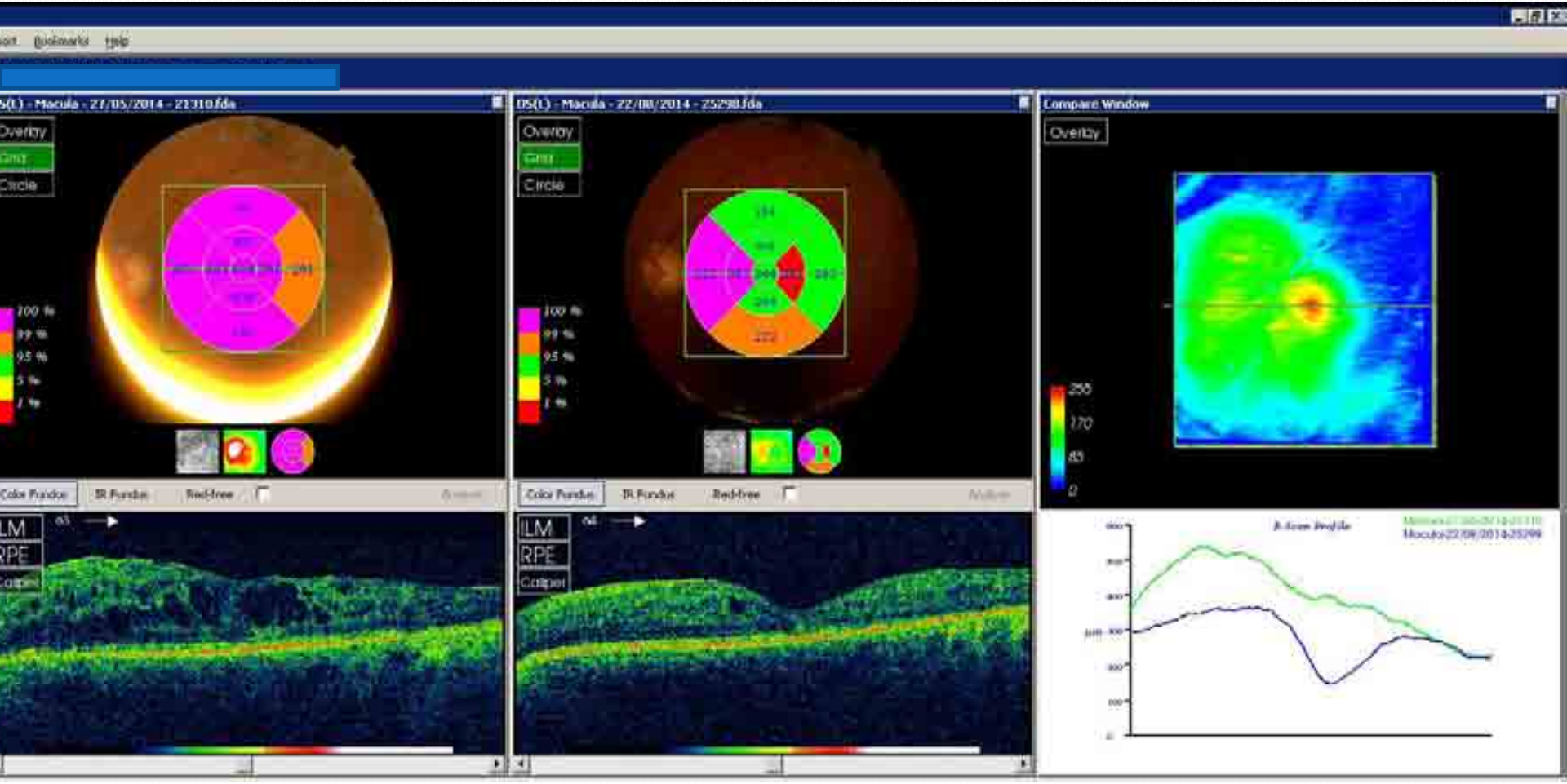
3/2/14 10/2 14



SJ: 76 years type 2 - Iluvein left eye
previously avastin (3) and triamcinolone 1
on azopt after triamcinolone
no extra IOP lowering treatment needed after Iluvein



SH, type 1, renal pancreatic transplant. R eye responds to anti Vegfs, left vitrectomised eye does not. On Asopt BD before Iluvein. No extra drops needed



Points to ponder !!

- The patients appreciation of their visual improvement is more marked than the post injection visual acuity and OCT would suggest
- more accurate Logmar??
- anything else ? (contrast sensitivity)
- reflection of consultants enthusiasm??
- no unmanagable IOP rises to date (6 month follow up)
- process of dealing with the need for Iluvien in the phakic patient??
- Cataract surgery and Iluvien same day??
- Subsequent injection after surgery ??

New dawn of treatments for our patients