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ABSTRACTS COLLECTION

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RF1 Twelve-month outcomes of aflibercept versus ranibizumab for neovascular age-related macular degeneration (AMD)

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Background To directly compare visual acuity (VA) outcomes in year 1 of treatment with aflibercept vs. ranibizumab for eyes with neovascular age-related macular degeneration (AMD) treated in two centres by two different treatment regimens (Aflibercept (fixed-dosing every 8 wk) vs. ranibizumab (Treat and Extend)).

Methods Bi-centre retrospective data analysis from an electronic medical record (EMR) system. Hundred treatment-naive eyes with neovascular AMD received therapy with aflibercept or ranibizumab intravitreal injections (IVI). Eyes were matched at baseline for visual acuity (VA) and age. In Group A (University Hospital Southampton: 51 eyes) aflibercept was used as per a modified eight weekly protocol based on that in the VIEW studies (VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet AMD) [1] with a total of three Clinic Visits (three optical coherence tomography (OCT) exams) during a year of treatment (Fig. 1a). In Group B (West Suffolk Hospital: 49 eyes) ranibizumab was used per a Treat and Extend (T&E) protocol: a loading of 3 IVIs performed, followed by monthly injections till maximum VA and anatomic outcome was observed. Then, the inter-IVI interval was extended/shortened by 2 weeks based on disease activity (Fig. 1b). Mean change in best-corrected visual acuity (BCVA) and central retinal thickness (CRT) at year 1 compared to baseline, mean number of injections and visits were collected. Economic analysis was performed based on data from the coding department.

Results Baseline parameters were well matched (Age, baseline BCVA and CRT). The mean VA of Aflibercept-treated eyes improved from 0.49 log of the Minimum Angle of Resolution (LogMar) at baseline to 0.34 LogMar ($+7.5$ ETDRS L gain ($P = 0.0010$)) at end of year 1 (Y1), compared with 0.48 LogMar at baseline to 0.32 LogMar ($+8.3$ ETDRS L gain ($P < 0.0001$)) for Ranibizumab-treated eyes. Mean BCVA Group A vs mean BCVA Group B ($P = 0.1550$).

The mean BCVA gain of Group A was comparable to VIEW 1 and 2 Trials' results at end of Year 1 [1]. The mean BCVA gain of Group B was comparable to the cohort receiving a treat and extend posology in TREX-AMD 1-Year Results [2]. The mean CRT of Group A improved from 354 µm at baseline to 214 at Year 1. The mean CRT of Group B improved from 428 µm at baseline to 272 at Year 1. In aflibercept-treated eyes, at end of Year 1, 24/51 (46%) eyes had a dry macula with a mean BCVA of 0.41 LogMar vs. (27/51; 54%) eyes with BCVA of 0.36 LogMar in which the macula was deemed to be active ($P = 0.0467$). Inactive disease was defined by the absence

of intraretinal (IRF) or subretinal fluid (SRF) on macular OCT scan, whereas active disease was defined by the presence of macular haemorrhage, SRF, IRF or intraretinal cysts (IRC) on spectral domain SD-OCT scan. Table 1 shows multiple parameters compared between the two groups with their statistical significance. Economic analysis revealed the total mean cost per patient per annum was £6919.00 for aflibercept per Southampton protocol, £7395.00 for ranibizumab per the T&E protocol, see Table 2.

Conclusions Visual gains were significant and comparable for both Aflibercept (Q8W) and Ranibizumab (T&E) used proactively in year 1. In the Treat and Extend group (ranibizumab), the choroidal neovascularization (CNV) lesion was graded as inactive at a mean inter-injection interval of 9.5 weeks (range 6–12). In the Aflibercept-treated group, 54% of the eyes were deemed to be active at end of Y1. Active lesions (mean BCVA at month eleven was 0.36 LogMar) did not have worse VA outcomes compared with inactive lesions (mean BCVA at month eleven was 0.41 LogMar) ($P = 0.0467$). From an economic point of view, one of the factors responsible for the difference of the total cost of treatment between both drugs in favour of Aflibercept is the number of office visits. A virtual setup where less office visits are performed could make ranibizumab-Treat and Extend a competitive cost effective option for treatment in Y1 in AMD patients.

Acknowledgment The prices noted in this analysis were accurate at the time of review, however the current list price for Lucentis (ranibizumab) is £551 per injection and has been since June 2016. In practice, both aflibercept and Lucentis prices are subject to a Patient Access Scheme as part of the NICE appraisal whereby the cost to centres is significantly discounted [3]. Costs of different procedures and different types of visits were facilitated by local coding department and represent costs locally agreed with commissioners. Data are available from the corresponding department on request through freedom of information (FOI) request (freedomofinformation@uhs.nhs.uk).

Clinical Trial Registry VIEW 1 (registered at www.clinicaltrials.gov on July 31, 2007; NCT00509795. W 2 (registered at www.clinicaltrials.gov on March 12, 2008; NCT00637377. The Treat-and-Extend Protocol in Patients with Wet Age-Related Macular Degeneration (TREX-AMD) (registered at ClinicalTrials.gov on December 12, 2012;, NCT01748292).

Disclosures HA received consulting fees and lecture fees from Bayer and Novartis. LM received lecture fees from Novartis and Bayer. AV received consulting fees from Novartis and Bayer, and lecture fees from Novartis. AL received consulting fees from Bayer and serves as the EIC for Eye.

References

1. Heier JS, Brown DM, Chong V, Korobelnik JF, Kaiser PK, Nguyen QD et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology 2012;119(12):2537–48.
2. Wykoff CC, Croft DE, Brown DM, Wang R, Payne JF, Clark L et al. Prospective trial of Treat-and-Extend versus Monthly Dosing for neovascular age-related macular degeneration: TREX-AMD 1-Year Results. Ophthalmology 2015;122(12):2514–22.
3. Joint Formulary Committee. British National Formulary 74. London: BMJ Group and Pharmaceutical Press; 2017. P.1090.

Table 1 [RF1]: Principal outcomes: Group A (aflibercept) vs Group B (Ranibizumab)

Characteristic	Group A (Aflibercept)	Group B (Ranibizumab)	*P* value	95% Confidence interval
Mean Baseline VA LogMar (SD)	0.49 (0.16)	0.48 (0.17)	$P = 0.9$	−0.07195 to 0.06321
Mean VA LogMar End of Y1 (SD)	0.34 (0.21)	0.32 (0.19)	$P = 1.00$	−0.0801 to 0.0801
Mean VA gain in Y1 (ETDRS letters)	+7.5 L	+8.3 L		
Mean (SD) Baseline CRT microns	354 (121)	428 (152)	$P = 0.46$	−186.81 to −78.01
Mean (SD) CRT End of Y1 microns	214 (65)	272 (67)	$P < 0.0001$	−84.55 to −32.02
Mean (SD) #IVIs	7 (0.0)	7.75 (1.22)	$P < 0.0001$	−1.09 to −0.42
Average # office visits	3 (0.0)	5.75 (1.22) Range 5-11	$P < 0.0001$	−3.10 to −2.41

Table 2 [RF1]: Economic analysis

Dosing protocol	Group A modified VIEWQ8W	Group B Treat and Extend
Drug	Aflibercept	Ranibizumab
Cost of drug per IVI (£)[3]	816	742
Mean number of doses per year	7	7.75
Mean number of outpatient visits with OCT, VA and IVI (£245)[4]	3	5.75
Mean number of outpatient visits with VA (£118)[4]	4	2
Total mean cost of treatment (£)	6919.00	7395.00

Fig. 1 **[RF1]**: Treatment Regimens for (**a**) Aflibercept per modified VIEW protocol in Centre A, (**b**) Ranibizumab per Treat and Extend in Centre B. Yellow circles represent an injection + OCT scan visit. The injection symbol represents an injection-only clinic

RF2 Intravitreal ranibizumab for the treatment of macular oedema associated with branch retinal vein occlusion (BRVO): Results for 3 years

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Background The technology appraisal guidance (TAG) [1] concerning the use of ranibizumab in the treatment of visual impairment caused by macular oedema secondary to Branch retinal vein occlusion was published by the national institute for health and care excellence (NICE) in May 2013 and has been available to NHS patients since late 2013.

We report our results for three years from April 2014 to April 2017 at Princess Alexandra Hospital (PAH), Harlow. The current regimen used at PAH is the Treat and Extend (T&E), which was implemented following the update to the Ranibizumab license in 2014.

The aim of our audit is to determine the visual acuity (VA) outcomes and injection frequency of intravitreal Ranibizumab in patients with BRVO with macular oedema. To assess percentage of eyes achieving defined visual acuity and driving vision.

Methods Retrospective review and analysis of patient data were carried by use of Medisoft software. It included the 3 year data between April 2014 and April 2017.

Results All patients received an intravitreal Ranibizumab initial loading dose of five injections or until demonstrating a stable VA for 3 visits, which was then followed by a treat and extend regimen. A total of 101 patients and 103 injections were administered. Two patients developed bilateral disease during the course of treatment. A total of 111, 317, 306 and 75 injections were administered during the years of 2014, 2015, 2016 and 2017, respectively (Fig. 1). Patients received an average of seven injections in the first year, followed by four in the second year (Fig. 2). The frequencies of visits are 9.4 in the first year and 6.9 in the second year (Fig. 3). The mean baseline VA was 55 letters. At 35 months, the mean VA was 75 letters which was a 20 letter gain in our patients. At 6 months, 70.5%, 49.2% and 34.4% of eyes gained ≥5 letters, ≥10 letters and ≥15 letters, respectively. At 30 months, 71.4%, 71.4% and 42.9% eyes gained ≥5 letters, ≥10 letters and ≥15 letters, respectively (Fig. 4). Percentage of eyes achieving more than 70 letters was 60% at 12 months and 57.14% at 30 months (Fig. 5).

Conclusion In the RETAIN [2] study, mean VA was 74.1 letters at 4 years, an improvement of 20.1 letters from baseline (mean baseline VA 54 letters) as compared to 20 letters from baseline (mean VA 55 to 75 letters) at 35 months in our study (Fig. 6) (Table 1). Mean number of injections in PAH was 7 in the first year as compared to 8.4 in RETAIN and 8.3 in BRAVO (Table 1). Less number of injections administered in PAH in the first year as compared to RETAIN study can be explained by the treat and extend regimen.

More than half of eyes treated in PAH achieved driving vision at 30 months. Long-term outcomes of BRVO patients treated with Ranibizumab are comparable to BRAVO and RETAIN studies.

Disclosure The authors have declared no conflicts of interest.

References

1. National Institute for Health and Care Excellence (UK) Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion – available at https://www.nice.org.uk/guidance/ta283. Accessed Oct 2017.
2. Campochiaro PA, Sophie R, Pearlman J, Brown DM, Boyer DS, Heier JS et al. Long-term outcomes in patients with retinal vein occlusion treated with ranibizumab: the RETAIN study. Ophthalmology. 2014;121(1):209–19.

Table 1 [RF2]: Comparison of key results from published studies and PAH

Comparision of results from BRAVO, RETAIN and PAH			
Criteria	BRAVO	RETAIN	PAH
Improvement of mean VA from baseline	16.7 letters (12 months)	20.1 letters (4 years)	20 letters (35 months)
Frequency of injections	8.4 in 1st year	8.3 in 1st year	7 in 1st year

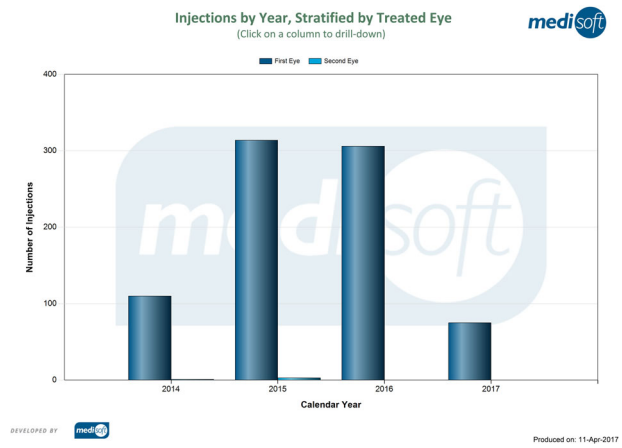

Fig. 1 **[RF2]**: Injections by year Graphical outputs from Medisoft's audit software mediSIGHT® are reproduced with permission. © Copyright 2017 Medisoft Limited

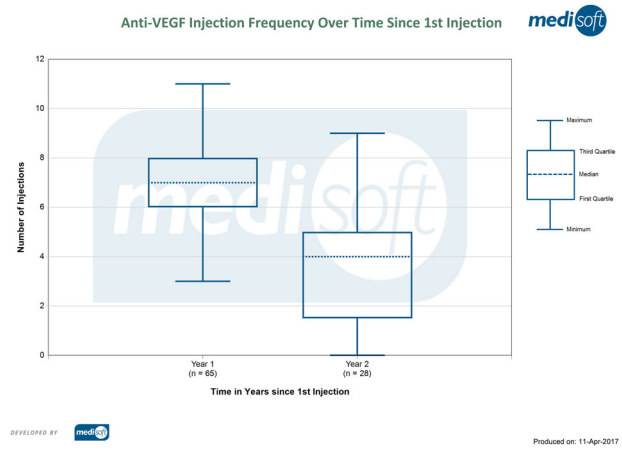

Fig. 2 **[RF2]**: Injection frequency over time Graphical outputs from Medisoft's audit software mediSIGHT® are reproduced with permission. © Copyright 2017 Medisoft Limited

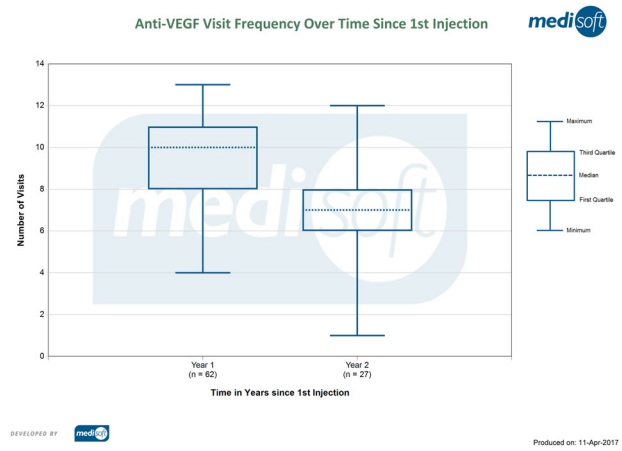

Fig. 3 **[RF2]**: Visit frequency over time Graphical outputs from Medisoft's audit software mediSIGHT® are reproduced with permission. © Copyright 2017 Medisoft Limited

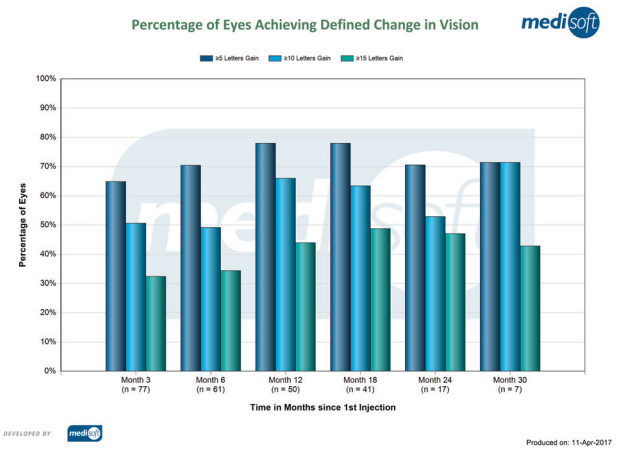

Fig. 4 **[RF2]:** Proportion of eyes achieving defined VA Graphical outputs from Medisoft's audit software mediSIGHT® are reproduced with permission. © Copyright 2017 Medisoft Limited

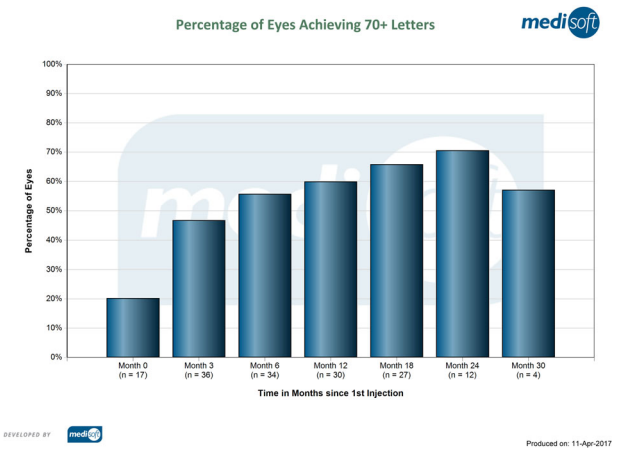

Fig. 5 **[RF2]:** Proportion of eyes achieving driving VA Graphical outputs from Medisoft's audit software mediSIGHT® are reproduced with permission. © Copyright 2017 Medisoft Limited

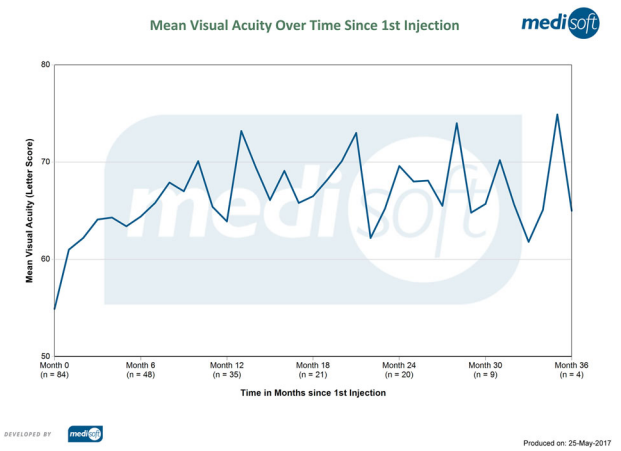

Fig. 6 **[RF2]**: Mean VA over time Graphical outputs from Medisoft's audit software mediSIGHT® are reproduced with permission. © Copyright 2017 Medisoft Limited

RF3 Withdrawn

RF4 An Audit of in-house prescription errors from the emergency eye department and the impact on resources and patient care of any errors

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Background Patients attending eye casualty are often prescribed medications as written prescriptions that have the potential to contain errors or being incomplete, generating extra work for prescribers and pharmacists, increasing risk of patient harm and delaying both treatment and discharge from the eye department. This audit was performed by Ophthalmic Pharmacists and the Ophthalmology Team to determine the number of errors in prescriptions and to obtain information about the magnitude and type of problems caused by these errors to quantify the impact on pharmacy staff resources. The locally derived standard against which the audit was to be measured was that there should be no prescription errors.

Methods Data were prospectively collected for five consecutive days in April 2017 (Monday till Friday) when the Eye Pharmacy was receiving prescriptions from the adjoining emergency eye department. Ophthalmic staff issuing prescriptions during this period were unaware of the audit. All prescriptions were analysed for errors, omissions or any other problems but details of the prescriber were not captured.

The time spent by the pharmacist to resolve the problems created by identified errors on prescriptions was also recorded in a standard data collection form. A previous feasibility study had been performed to streamline the data collection process and identify potential issues prior to conducting this audit and had facilitated the process.

Results During the five day audit period 225 prescriptions from the eye department were dispensed by the eye pharmacy. Of these 86 (38.2%) had problems that required the pharmacy to contact the prescriber. Fifty-three (62%) of the problem prescriptions were resolved in under 5 min usually by face to face contact with the prescriber, 21 (24%) were resolved in between 5 and 10 minutes, and a smaller number, 11 (13%) took between 10–20 min to resolve. One prescription took between 15 and 20 min to resolve.

Between 6.5 h per week and 11 h per week of pharmacy staff time was taken up in contacting prescribers about the prescriptions they had written. The 6.5 h per week was based upon an average of 3 min for the prescriptions resolved between 5 and 10 min and the lower limit of the other time ranges—5 min, 10 min and 15 min. Eleven hours per week was calculated using the upper limit of the time ranges in the results obtained.

The most common reason for contacting the prescriber was illegibility of the prescription followed by the need to clarify which eye the medication was intended for. Some prescriptions had more than one problem that required resolution (Table 1).

Recommendations as a result of the audit included electronic prescribing which may reduce errors from illegible hand-written scripts. The education of prescribers about such errors and omissions through training sessions at induction and at other opportunities as well as using posters in the department may have further positive impacts.

The audit should be repeated regularly. The benefit of reducing prescribing errors may free up time for pharmacists, minimise costs to the Trust, and reduce both the inconvenience and possibility of harm to patients. A typed and structured prescription template with a list of the commonly prescribed medicines and routes of administration can be used to see if it reduces errors. This template may also be useful for contingency planning in the event of an IT failure affecting any future Electronic Prescribing.

Our action plan includes the institution of Electronic Prescribing with help from the Trust by the end of this year, and a repeat of the audit once the electronic prescribing is in place. The audit team is to produce small posters highlighting key points of the audit and display at workstations for education of all those working in the emergency eye department.

Conclusions The audit has identified there is a need to improve the quality of prescriptions written by ophthalmic prescribers. Although many of the errors identified were minor and were resolved without significant delay, the cumulative impact of such a large number of errors, however minor, could result in over 6 h of the pharmacist's time to resolve during the 5 days audit period. As well as the impact of staff resources there were also financial implications where prescribers were prescribing items not on the formulary. The delays in resolving the prescribing errors resulted in patients remaining in the eye department for longer periods of time than was necessary. All errors were correctly identified and dealt with effectively therefore no patient came to harm.

Disclosures SK received lecture fees from Santen Ltd. PP received support from Alcon (A Novartis company. The remaining authors declared no competing interests.

Table 1 [RF4]: Key results from audit

Date	Monday	Tuesday	Wednesday	Thursday	Friday	Total
Total daily A&E prescriptions	49	45	47	38	46	225
Total daily problematic prescriptions	21	17	16	14	18	86
Queries/ Intervention						
Medication				1	1	2
Formulation	1		1			2
Strength	1		2	1		4
Eye	5	1	2	6	5	19
Route of administration	1					
Dose	2	3	2	1	2	10
Duration	1	1	1			3
Contraindicated	1					1
Other						
Date	2					2
Name & address of patient			2			2
Formulary	4	4	1	2	4	15
Identifiable signature	1					1
General legibility	2	6	4	3	7	22
Supply problem	2		1	1		5
Inappropriate Hospital number (OPD/A&E)	1	1		3		5
Total time taken to resolve						
<5 min	13	12	10	4	14	53
5–10 mins	4	4	3	7	3	21
10–15 mins	4	1	3	2	1	11
15–20 mins				1		1
Total number of errors per prescription						
1 error	18	17	16	10	17	78
2 errors	3			4	1	8

RF5 Pressure points

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Background Tonometry is the measure of the intraocular pressure in the eye. It is an essential part of ocular assessment, diagnosis and prognosis in Ophthalmology. The gold standard device for this kind of measurement is the Goldmann tonometer. Portable intraocular pressure testing devices offer convenience and require little operator training; so for the majority of cases portable tonometry devices are adequate, however where precision is crucial, ophthalmologists and secondary care practitioners rely on the gold standard Goldmann Applanation Tonometer.

The Goldmann tonometer is a slit lamp bio-microscope add-on device, mounted on a plate in front of both the viewing and lighting systems. After the insertion of a topical anaesthetic and fluorescein eye drops, the slit lamp is advanced forward towards the cornea to enable a measurement to be taken. Based on the Imbert-Fick Law [1], of a perfectly dry, spherical and infinitely thin sphere, the pressure is equal to the force required to flatten the sphere, divided by the area being flattened. These variable factors alone, limit the accuracy.

There are a number of confounding factors that can influence the measurements of the gold standard tonometer. These can include the amount of fluorescein inserted, corneal thickness, astigmatic error and pressure on the globe [2] (Table 1). Errors of precision can be minimised by adjusting for these factors in examination or calculation.

However, a step that is often omitted is calibration of the tonometer [3]. As with all factors influencing intraocular pressure measurements, tonometer calibration should be carried out regularly complying with manufacturer's guidelines to ensure the optimum performance and thus accuracy of the device. Haag-Streit, manufacturers of the Goldmann Tonometer, recommends that measured calibration errors of greater than ±0.5 mmHg should be returned to the manufacturer [4].

The accurate measure of intraocular pressure has been outlined as the main risk factor for glaucoma [5] therefore the accuracy of tonometry readings is vital in management. Sandhu et al's study, measuring the length of time required between calibration checks noted that at one month after recalibration by the manufacturer, only 2 Goldmann tonometers fell within the recommended range, with 0 at month four. Their results also demonstrated that over 40% of tonometers had errors over ±2.5 mmHg within the first month. They explain that errors of ±2.5 mmHg is a clinically acceptable error margin with the responsibility falling on the ophthalmologist prior to use before clinical sessions [6].

There is no known, gold standard clinical guideline or protocol recommending how often and with what error, tonometers should be calibrated within a department. Currently individual local protocols are generally used, but these can vary widely from annual calibration, to more frequent checks for best practice [6–8][6]. Choudari et al reports that older tonometers are more at risk of calibration errors. He suggests that newer tonometers can be checked twice yearly and older tonometers monthly [9].

Currently, other that the 0.5 mmHg recommended error allowance by Haag-Streit, there is no universally accepted error threshold. One constraint is that Goldmann tonometer dial markings only enable accurate measurements of 2 mmHg increments. Therefore, in the interest of accuracy and pragmatism, a target of 1 mmHg would be more realistic, allowing an approximation between the measurement bars to be made.

Lastly, in Kumar's study, one hundred busy, resident ophthalmologists attending the Royal College of Ophthalmology Congress were asked about tonometry calibration. Seventy percent did not either feel or appreciate that "tonometer checks might be their responsibility" and thought that a nurse or alternate staff member should ensure their accuracy was maintained. The structured questionnaire also demonstrated that 85% had never performed calibration checks, whilst only 7% checked prior to the start of each clinical session. Kumar suggested that that responsibility of calibration checks should be designated to a defined and known individual in order to ensure the accuracy of equipment is maintained [10].

Methods Our aim was to create a protocol for monthly tonometer calibration check with recording of error each month by a designated staff member. As part of the protocol it was our intention that all outpatient department Goldmann applanation tonometers at Oxford Eye Hospital would be calibrated within ±1mmHg as per best practice for intraocular pressure measurements on a monthly basis. Additionally the service date for each tonometer would be recorded and any tonometer not meeting the recalibration guidelines would be returned to the manufacturer as per guidelines for recalibration.

We implemented the method outlined by the manufacturer of Haag-Streit Goldmann Applanation tonometers [4] to assess calibration of the 11 tonometers in the outpatient department at Oxford Eye Hospital. This required the dial to be turned in a clockwise rotation for the 1st measurement and anti-clockwise rotation for the 2nd measurement and then the readings averaged. Those Goldmann tonometers that were not calibrated within ±1 mmHg, or due for service were returned to the manufacturer. The Tonometer calibration was re-audited one month later.

Results (see Fig. 1 **& Fig**. 2) 45% of Goldmann Applanation tonometers were calibrated within ±1mmHg whilst 4 out of 11 required servicing as per servicing expiry dates noted on the tonometer, and 6 were sent to the manufacturer for recalibration. At 0 the calibration error ranged from 0 mmHg to + 4 mmHg, at 20 from + 20 mmHg to + 28 mmHg and at 60 from + 57 mmHg to + 63 mmHg.

Discussion All outpatient department Goldmann Applanation tonometers at Oxford Eye Hospital were found to be within calibration limits of ±1 mmHg at the re-audit. As part of the initial audit a draft proforma was introduced in the form of a logbook to be filled in for each tonometer on a monthly basis with the recording of the measurement for each tonometer. The draft protocol incorporates monthly review of tonometer calibration throughout the department, and that any Goldmann Applanation tonometer identified to lie outside specified calibration limits should be sent to the manufacturer for servicing and recalibration and tonometers should be sent for regular servicing as per the manufacturer's instructions.

In this audit the Foundation Year 2 doctor completed the calibration testing. Although nursing staff were aware of the need to perform tonometer calibration, due to time constraints, similar to doctors, they were not able to complete the task. Some nurses explained that they tested for the rocking of the tonometer head at "0" prior to each clinic commencing and thought that this was sufficient. Other speciality doctors and fellows in the department explained that the calibration in other hospitals had not been their responsibility and thus had assumed that it was being carried out regularly. It is clear from this audit and others that the responsibility for tonometry calibration checks needs to be defined but will depend on local guidelines.

This audit showed how important calibration is, and without this how variable the measurements can be. In a busy department, without this being specified as part of routine equipment maintenance, its importance may be overlooked.

Disclosures SD served as a consultant for Circadian Therapeutics and has received grant support from RPFighting Blindness, Wellcome Fight for Sight, and National Institutes of Health Research (NIHR).

Table 1 [RF5]: The effect of variables on the measure of intraocular pressure

The effect of each confounding variable on the intraocular pressure measurement by a Goldmann applanation tonometer

Issue?	Increase or decrease?
Thick cornea	↑
Thin cornea	↓
Steep cornea	↑
Flat cornea	↓
Morning	↑
Night	↓
Holding your breath	↑
Holding the lid open	↑
Too much flurorescein	↑
Too Little flurorescein	↓
Human error	Variable

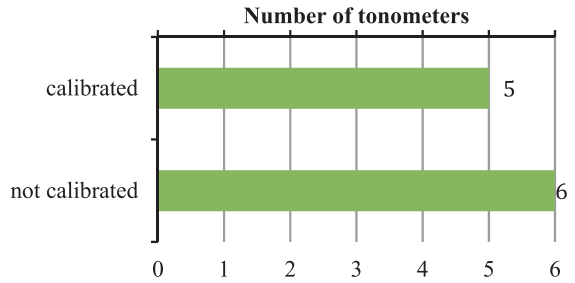

Fig. 1 [RF5]: Pre-intervention calibration status

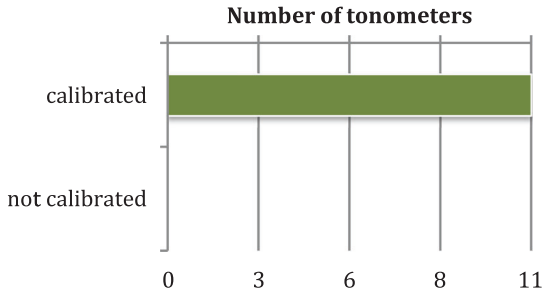

Fig. 2 [RF5]: Post-intervention calibration status

References

1. Mark HH. Armand Imbert, Adolf Fick, and their tonometry law. Eye. 2012;26(1):13–6.
2. Whitacre M. and Stein R. Sources of error with use of Goldmann-type tonometers. Surv Ophthalmol. 1993; 38(1):1–30.
3. Kumar N. and Jivan S. Goldmann applanation tonometer calibration error checks: Current practice in the UK. Eye 2006;21(6):733–4.
4. Haag-Streit. Goldmann Applanation Tonometer "How to check tonometer calibration" Available at: https://www.haag-streit.com/fileadmin/Haag-Streit_USA/Diagnostics/tonometry/download/procedures-for-checking-tonometer-calibration.pdf. Accessed on 27 January 2017.
5. Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthal. 2002;120(6):829–30.
6. Sandhu SS, Chattopadhyay S, Birch MK, Ray-Chaudhuri N. Frequency of Goldmann applanation tonometer calibration error checks. J Glaucoma. 2005; 14(3):215–8.
7. Choudhari NS, George R, Baskaran M, Vijaya L, Dudeja N Nikhil S. Measurement of Goldmann applanation tonometer calibration error. Ophthalmology. 2009;116:3–8.
8. Kumar N and Hillier RJ. Goldmann tonometer calibration: a national survey. Eye. 2009;23(2):413–5.
9. Choudhari NS, Rao HL, Ramavath S, Rekha G, Rao A, Senthil S et al. How often the Goldmann applanation tonometer should be checked for calibration error? J Glaucoma. 2006; 25(11):908–13.
10. Kumar N. and Jivan S. Goldmann applanation tonometer calibration error checks: Current practice in the UK. Eye. 2006;21(6):733–4.

RF6 Ranibizumab in neovascular age-related macular degeneration (AMD); twelve-month outcome of treat and extend regime at Wolverhampton and Midland Counties Eye Infirmary

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Background There are estimated to be 40,000 new cases of neovascular age-related macular degeneration (AMD) in the UK each year [1]. There are currently various anti-VEGF injection regimens employed to manage these patients which include; monthly injections, as required (PRN) injections and treat and extend (T&E). There is a consistent effort to ensure that any regimen is optimised by reducing over or under treatment to enable maximum efficient use of hospital eye service (HES) resources. The T&E regimen has the additional benefit of being a "one stop" service, with injections and assessments being administered at the same clinic appointment. The purpose of this audit was to determine if the T&E pathway (Fig. 1) can improve and stabilise patient outcomes when compared with PRN, and to provide some evidence by which workload can be more effectively predicted

Methods 25 consecutive eyes from 23 patients who were treatment-naive to T&E were audited in 2015, selection was based on completion of 12 months on the T&E pathway and data collection was retrospective from patient medical notes. Criteria assessed included number of letters read, number of injections and choroidal neovascular (CNV) activity for each visit over a 12 month period.

Results Baseline characteristics and outcomes at 12 months are reported in table one. Lesion type is defined in Fig. 2. This study provides a small real life snap shot of using T&E in practice, albeit with a small patient group. We have demonstrated an average letter gain comparable to the Hatz study [2] in Fig. 3. The number of dry episodes achieved is slightly higher than both the CATT study—ranibizumab PRN arm (19.25%) and the CATT study ranibizumab monthly arm (45.5%)[3]. This audit did demonstrate a slightly higher number of clinic visits and

injections over 12 months when compared to Hatz T&E, however our sample size is significantly smaller (Fig. 4).

Conclusions: The T&E model is a viable option, maintaining good outcomes at 12 months. This can potentially reduce the burden to both the HES and the patient by reducing the amount of visits required to the HES clinics. It should be noted however, that not all patients are suitable for T&E, as some lesions will settle after the initial loading dose and require no further treatment. There is also some caution with persistently over treating a "dry" macular due to the risk of atrophic changes.

Our recommendation is to repeat the audit with a larger sample size and a longer period of follow up. It is anticipated with this real world data we may be able to demonstrate patterns of injections regimens for different lesion types and better predict workload in addition to managing patient expectation.

Disclosure CP declared no competing interests. MK received lecture fees from Novartis Pharmaceuticals. NN received consulting fees from Bayer and Novartis, and lecture fees from Novartis. YY received consulting fees from Novartis and Allergan, and lecture fees from Novartis, Bayer and Allergan.

References

1. Owen CG, Jarrar Z, Wormald R, Cook DG, Fletcher AE, Rudnika AR. The estimated prevalence and incidence of late stage age-related macular degeneration in the UK. Brit J Ophthal. 2012;96(5):752–6.
2. Hatz K and Prunte C. Treat and Extend versus Pro re Nata regimens of ranibizumab in neovascular age-related macular degeneration: a comparative 12 month study. Acta Ophthalmology. 2017;95:e67–72.
3. Martin DF, Maguire MG, Fine SL, Ying GS, Jaffe GJ, Grunwald JE et al. Ranibizumab and Bevacizumab for treatment of neovascular age-related macular degeneration: 2-year results: Comparison of Age-related Macular Degeneration Treatment Trials (CATT) Research Group. Ophthalmology. 2012;119(7):1388–98.

Table 1 [RF6]: Baseline characteristics and results overview

Criteria	Result
Mean age at baseline (Years)	78.2 (±5.92)
Mean Baseline Visual Acuity (VA)ETDRS letters	57.24 (±12.24)
Male/female number (percentage)	16 (64%): 9 (36%)
Month 12 mean VA change form baseline ETDRS letters	+7.64 (±9.99)
Percentage with ≥ 15 ETDRS letters gain	12% (3/25)
Percentage with ≤ 15 ETDRS letters loss	100% (25/25)
Percentage with "dry episodes"[a]	54%
Percentage with no "dry episodes"[a]	20%
Percentage dry at every visit and extended	16%
Percentage achieving between 60–85% "dry episodes"[a]	48%

[a]Determined by no activity of the CNV lesion

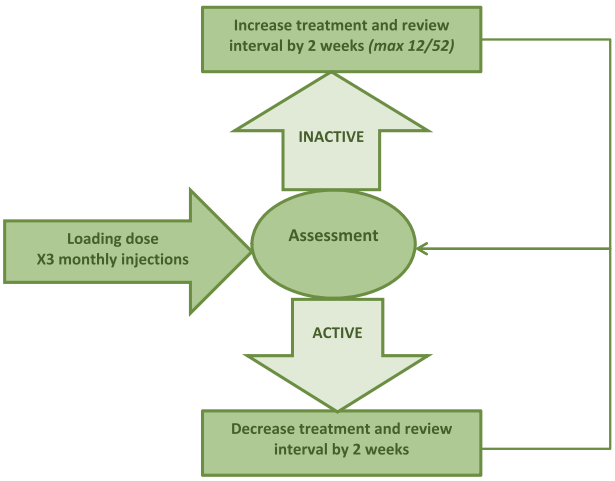

Fig. 1 [RF6]: Flow diagram of T&E pathway

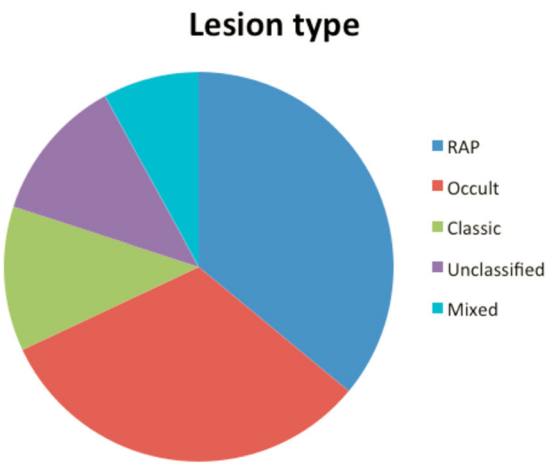

Fig. 2 [RF6]: Diagnosis of lesion

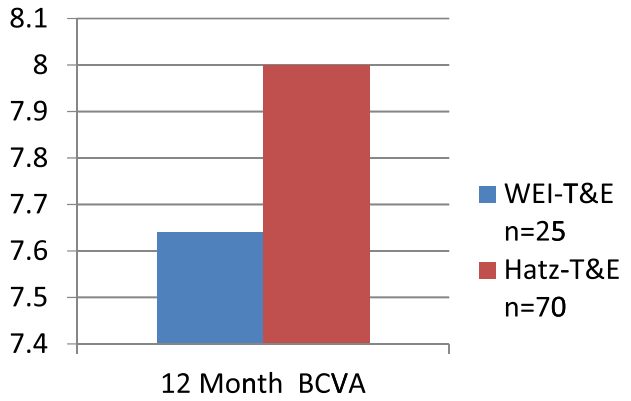

Fig. 3 [RF6]: 12 month BCVA comparison with Hatz study

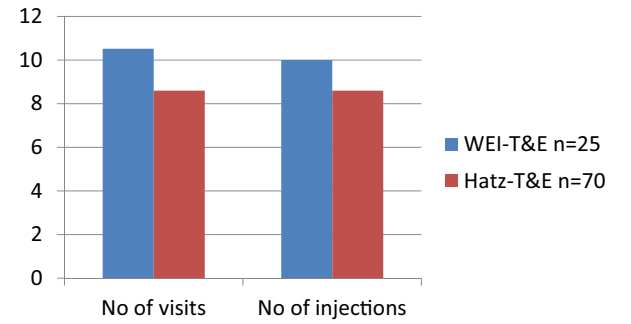

Fig. 4 [RF6]: Comparison of number of visits and injections with Hatz study

RF7 Re-audit of 2-year outcomes of 'When required' (PRN) Ranibizumab treatment of wet age-related macular degeneration (wAMD) in Fife National Health Service (NHS)

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Background Audit of the visual acuity outcomes of patients 2 years after the initiation of their ranibizumab treatment was last performed in 2014. The results compared favourably with recognized real world audit standards [1, 2]. Our system is straightforward for all team members to follow; all patients received three ranibizumab injections initially, then PRN injections based on defined changes to optical coherence tomography (OCT), photograph appearance or visual acuity (VA) at regular nurse-led or doctor review clinics. Subsequent intravitreal injection (IVT) is usually with ranibizumab; some patients are switched to aflibercept at physician's discretion. To cope with the anticipated rise in demand, some changes were made to the service in 2014, including the introduction of a nurse injector, additional nurse-led clinics and altering two doctor-led clinics to be partially one-stop. Most clinic episodes remain two stop; after assessment the patient is brought back to have their injection at a later clinic.

Methods Our aim was to ensure that the good results seen in 2014 are being maintained. A re-audit of the 2-year visual acuity results of a new cohort of wet AMD patients who began ranibizumab treatment in 2014 were audited against the same standards as before. The standards we compared were:

Mean change in Best Spectacle Corrected VA (BSCVA) (or pinhole VA, if better) 2 years after starting ranibizumab treatment (+1 letter) [1], The proportion of patients who had VA of 0.3 LogMar or better at 2 years (30%) [1], and the mean time between receipt of referral and 1st clinic and between 1st clinic and first injection (14 days total) [2].

The names of all treatment-naive NHS Fife patients who initiated IVT (all given ranibizumab) for wAMD were prospectively collected. Those starting IVT between May and August 2014 had their BSCVA data collected manually from the electronic patient record (EPR). In the previous audit, the EPR VA data were found to be 100% reliable when compared to the case note records, but the time from receipt of referral to first clinic and from first clinic to first IVT was often misleading, so for this audit, the case notes were obtained for patients for whom the EPR showed a long period to clinic or to IVT. The number of eyes studied and the period of enrolment was similar to the previous audit. The mean number of injections over 2 years was also collected from the EPR, though this is not an audit standard. To allow direct comparison with the real world audit standard, only patients who were still in the hospital eye service (HES) at the 2-year point had their data included in the audit. For interest the case notes of the excluded patients were examined. For the part of the audit dealing with times to 1st clinic and to 1st IVT, all patients who began IVT were retained in the audit, as there was no reason to exclude them.

Results For the period 1 May 2014–18 August 2014, 44 eyes of 43 patients were prospectively recorded as having initiated IVT for wAMD, after exclusion of five eyes on the grounds of either having a diagnosis other than wAMD, no initial VA, no IVT actually given, or because the patient was not a new patient. Ten eyes were excluded as there was no 2-year VA in the EPR or case notes, due to discharge or death of patient. The remaining 34 eyes of 34 patients were subject to the audit. All 44 eyes of 43 patients were analysed with regard to the elapsed time between receipt of referral and 1st clinic and between 1st clinic and 1st IVT (Table 3). Patient data with

unrealistically large times had a case note review performed and where appropriate, were excluded from the calculation of the mean values. Twenty-one eyes were excluded (leaving 23 eyes of 22 patients) from the time from referral to 1st clinic data for the following reasons; there was no new referral because patient was already attending a HES macula or other eye clinic, first visit was at non-macular clinic because wAMD not suspected from the referral letter, the eye had dry AMD at first visit or patient did not attend the first clinic. Eighteen eyes were excluded from the time from 1st clinic to 1st IVT (leaving 26 eyes of 25 patients) because Fluorescein angiography (FA) or Indocyanine green angiography (ICG) was ordered at first visit, the eye was dry at first visit or wAMD was picked up at routine follow-up of the treated fellow eye, producing a delay in treatment that was not due to capacity issues.

Conclusions Our small unit has consistently delivered VA results that compare favourably with the real world benchmarks for the treatment of wAMD with ranibizumab or aflibercept. Real world benchmarks are required as the VA results achieved in the clinical trials of wAMD treatment are almost never realized in practice, whether using fixed injection or PRN protocols. There is randomized controlled trial (RCT) evidence that there is no difference in visual outcome between fixed monthly dosing and PRN dosing [3]. In the real world, however, there is evidence that better visual results are obtained with fixed injections [4]. The VIEW study showed there was no difference in visual outcome between ranibizumab and aflibercept [5]. Our results, although with small numbers of patients and with different demographic and initial VA characteristics noted between the previous and current audits, indicate that it is possible to deliver good VA outcomes with PRN ranibizumab (Tables 1 and 2). This was achieved with a low number of injections.

Our emphasis is on providing high quality nurse-led monitoring clinics at not more than 6 week intervals and maintaining a close relationship with the patients – patients are encouraged to bring forward their appointment if their vision drops. The service is delivered by only 2 doctors, both of whom deliver some injections, 1 nurse injector and 3 or 4 registered nurses doing the nurse-led clinics. Other nurses, receptionists, referral screening staff and secretaries complete the close-knit team.

The increased number of nurse-led clinics and the shift to nurse-led injections has allowed us to maintain our follow-up interval at ~5 weeks and treat within 1–2 weeks, some patients are now also treated on a one-stop basis wherever possible. There has been no increase in the last 10 years in the number of macula clinical sessions provided by the 2 doctors who provide the service, despite a massive increase in demand for clinics, injections and for the checking of the nurse-led scans and case notes.

Our recommendation are that with the burgeoning IVT drug bill being under increased scrutiny and in the knowledge that demand for treatment will rise every year, that we will continue to use PRN ranibizumab, due to the low number of injections required to maintain good vision. We intend to train a second nurse injector. Clinic review intervals are being monitored—extra nurse-led clinics can be added in due course if necessary. More attention will be paid to discharging appropriate patients to optometry care and to not giving unnecessary treatment. We have not found it necessary to resort to fixed injections in an attempt to replicate the outcomes of randomized controlled studies with the disengagement of the patient from medical and nursing care that would entail. A re-audit will be done in due course, to ensure our results remain acceptable.

Disclosure AR received lecture fees from Novartis.

References

1. Writing Committee for the UK ARMD EMR Users Group. The nAMD database: multicentre study of 92 976 ranibizumab injections: report 1: visual acuity. Ophthalmology. 2014;121:1092–101.
2. Royal College Of Ophthalmologists. Age-Related Macular Degeneration: Guidelines for Management 2013. (cited 17 November 2017). Available from: https://www.rcophth.ac.uk/wp-content/uploads/2014/12/2013-SCI-318-RCOphth-AMD-Guidelines-Sept-2013-FINAL-2.pdf
3. IVAN Study Investigators, Chakravarthy U, Harding SP, Rogers CA, Downes SM, Lotery AJ, et al. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology 2012;119:1399–411.
4. Lee AY, Lee CS, Egan CA, Bailey C, Johnston RL, Natha S et al. UK AMD/DR EMR REPORT IX: comparative effectiveness of predominantly as needed (PRN) ranibizumab versus continuous aflibercept in UK clinical practice. Br J Ophthalmol. 2017;101(12):1683–8.
5. Heier JS, Brown DM, Chong V, Korobelnik JF, Kaiser PK, Nguyen QD et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology.2012;119:2537–48.

Table 1 [RF7]: Patient Demographics, VA Results and injections given in 2 years

	Current audit	Last audit	Benchmark audit
Mean age at presentation	79.2	76.8	79.9
Female/Male Ratio	2.8	1.1	1.7
Mean initial VA (LogMar)	0.49	0.64	—
Mean Final VA (LogMar)	0.41	0.52	—
Change in Mean VA (LogMar)	−0.08 (+4 letters)	−0.12 (+6 letters)	+1 letter
Mean number of IVT given in 2 years	6.6	7.3	5.7 in year one 3.7 in year two

Table 2 [RF7]: Mean VA outcomes with reference to the 0.3 LogMar VA benchmark

	Current audit	Last audit	Benchmark audit
% of eyes with mean VA of 0.3 or greater at presentation	44%	15%	15%
% of eyes with mean VA of 0.3 or greater at end of Year two	44%	41%	30%

Table 3 [RF7]: Time elapsed between receipt of referral to first clinic and between first clinic and first IVT

	Current audit	Last audit
Mean time from receipt of referral to first clinic visit (days)	10.00	9.96
Mean time from first clinic visit to first IVT (days)	9.77	9.06

RF8 Impact of a virtual diabetic referral clinic on waiting times

Rhianon Reynolds[1,*], Sarah Hale[1], Phillipa Knowles[1]
[1]University Hospital of Wales, Cardiff, Wales; *Presenter

Background In Wales, between 2005 and 2009, some 91, 393 people attended for first screening for diabetic retinopathy. There were 5003 Type 1 diabetics of whom 56% had "any diabetic retinopathy" reported, while 11.2% were noted to have "sight threatening diabetic retinopathy". Of the 86,390 patients with Type 2 Diabetes 30.3%, reported "any diabetic retinopathy" and "sight threatening diabetic retinopathy" in only 2.9%. The National Screening Committee (NSC) has Recommendations on the time between notification of a positive test and consultation. These are listed in Table1.

Method A previous audit within the University Hospital of Wales (UHW) in 2014 found that the mean routine referral to consultation time for retinopathy or maculopathy was 202 days (28.9 weeks). The range of referral time was between 97 and 328 days (13.9–46.9 weeks), and indicated that only 2.4% of referrals were being seen in an Ophthalmology clinic with the 18 week limit set by the national standard.

We initiated a pilot virtual diabetic retinopathy clinic at the UHW whereby following referral by the diabetic retinopathy screening service for Wales, the patient immediately receives an invitation to attend a clinic at UHW. At this clinic visual acuity is measured, pupils are dilated and macular optical coherence tomography (OCT) and OPTOS retinal imaging performed.The images obtained are reviewed remotely by an Ophthalmologist of Experienced Associate Specialist or Consultant level, and a decision made on the subsequent management of the patient.

Results The pilot was run between 2 January 2016–5 September 2016 and 106 patients were seen in this time. Of these patients whose ages ranged from 25–92 years, (mean 58.5 SD 13.88), 62 had maculopathy in 1 eye, 31 had bilateral changes and 13 had M0. Therefore there were a total of 186 eyes that had maculopathy at screening that required referral to the hospital eye service (HES).

Utilising the virtual clinic approach the mean screening to clinic time was 65.11 days (SD 18.9) equivalent to 9.3 weeks. However, as the mean delay in screening time to referral being received was 19.7 days (SD 16.3) equivalent to 2.8 weeks, if this taken into account referral to clinic time: can be considered as 44.8 days (SD 16.7 days) = 6.4 weeks (Fig. 1). It was found that the mean central retinal thickness was 257.4 μm (SD 48.26), 29 (12%) eyes showed cystic change—1 of which was referred with M0. A mean central retinal thickness of >400 μm was found in 4 patients (1.8%) (1 of which was due to ERM). LogMAR VA in these patients ranged from (0.24-HM)

Conclusions The pilot project of a virtual diabetic retinopathy clinic at UHW was shown to have significantly reduced referral to treatment times from 28.9 weeks to 6.4 weeks—well within the NSC guidelines. There were a number of patients benefits identified which include the identification of urgent cases, the reduction of "full"

outpatient clinic appointment requirements, as some 20% of referred patients were able to be discharged at the virtual clinic. Patients received a more prompt review and shorter hospital visits.

Disclosures RR received lecture fees from Novartis. SH and PK declared no competing interests.

Table 1 [RF8]: National Screening Centre recommendations for appointment timings

Urgent (R3AM0 R3AM1)	Routine (R2M0, R2M1, R1M1)
1a 60% < 2 weeks 1.b. 80% < 4 weeks	Minimum standard: 2a 70% < 13 weeks 2.b. 95% < 18 weeks
Achievable standard 1. 95% < 2 weeks	Achievable standard 2. 95% < 13 weeks

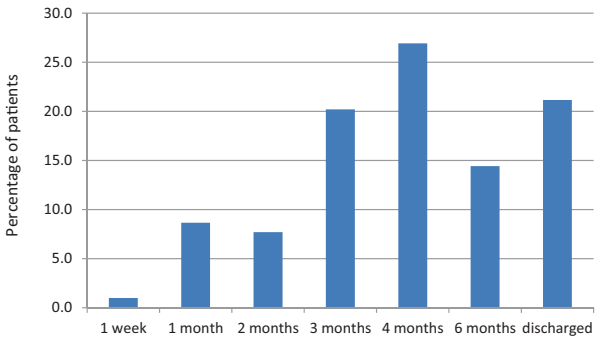

Fig. 1 [RF8]: Outcomes of virtual clinic—Next Appointment Given

RF9 Withdrawn

RF10 Ranibizumab treat and extend for neovascular age-related macular degeneration (AMD) - One-year outcomes

Dipti Trivedi[1], Fadi Alfaqawi[1,*], Peck Lin Lip[1], Bushra Mushtaq[1], Randhir Chavan[1];
[1]Birmingham and Midland Eye Centre, Birmingham, United Kingdom;[*]Presenter

Background The aim of our audit was to report our one-year data obtained through the use of a "treat and extend regime" with anti- VEGF therapy for the treatment of neovascular AMD. The results were compared to previously published "treat and extend" studies [1, 2].

Methods We included all treatment-naive patients who had completed 12 months on the treat and extend regime with anti-VEGF for neovascular AMD. Data were collected through retrospective review of patient notes and Medisoft system entries. The criteria to be compared included patient demographics, visual acuity (VA) and central retinal thickness (CRT) at a range of times (baseline, after the third injection, at 6 and 12 months).

The Treat and extend regimen: Patients received a "loading dose" of three intravitreal injections of ranibizumab, and were then seen at 4 weeks after the third injection. If "dry" on optical coherence tomography (OCT), the time to the next injection is extended to a period of six weeks—however, if they demonstrate any sub (SRF) or intraretinal (IRF) fluid they are injected at four weeks.

For subsequent visits injections are continued at four weekly intervals until the patient can be defined as "dry" whereupon the interval is extended in increments of 2 weeks up to a maximum extension of 12 weeks. If at any point the "dry" patient shows evidence of SRF or IRF, they are returned to a treatment interval of 4 weeks.

Results The patient group evaluated contained 23 patients with 25 eyes under treatment, 65% were female and 35% male with a mean age at baseline of 79 years (range 64–95). One of the evaluated patients showed persistent SRF despite therapy with Ranibizumab and treatment was changed to aflibercept. There was a range of lesion type treated, 44% were occult, 8% classic and 4% Retinal Angiomatous Proliferation (RAP) whilst 44% were unclassified. For visual and anatomic outcomes see Table 1. Figure 1 compares the local results with those from randomised controlled studies.

Conclusions The audit patient numbers were low but where, we feel, representative of the wider patient population. While the number of injections administered over a 12 months period was similar to that in published studies the visual acuity gains were less. This may be related to the lower baseline visual acuity of our cohort. We hope to repeat the audit with larger patient numbers and look at the number of "dry" episodes experienced by patients being treated with a treat and extend anti-VEGF regimen. We are consulting with the wider medical retina team with the aim of introducing a standardised treat and extend treatment pathway, to ease decision making in cases of recurrence.

Disclosures DT and RC declared no competing interests. FA and PLL received lecture fees from Novartis. BM has received consulting fees from Novartis, Bayer, Alimera, Lecture fees from Alimera sciences, Medical Educational Goods and Services (MEGS) grant support from Novartis.

References

1. Wykoff CC, Croft DE, Brown DM, Wang R, Payne JF, Clark Let al. TREX-AMD StudyGroup.

Prospective Trial of Treat-and-Extend versus Monthly Dosing for neovascular age-related macular degeneration: TREX-AMD 1-Year Results. Ophthalmology. 2015;122(12):2514–22.
2. Hatz K and PrünteC. Treat and Extend Versus Pro Re Nata regimens of ranibizumab in neovascular age-related macula degeneration: a comparative 12 month Study. Acta Ophthalmol. 2017;95(1):e67–72.

Table 1 [RF10]: Visual and anatomical outcomes

Criteria	Baseline	After loading dose	6 months	12 months
VA (ETDRS letters)	56 ± 16	61 ± 17	59 ± 15	64 ± 15
Change in VA from baseline (ETDRS letters)	—	+ 5 ± 12	—	+8 ± 13
Central retinal thickness (CRT) (microns)	398 ± 93	276 ± 54	259 ± 41	245 ± 39
Change in CRT from baseline (microns)	—	−123 ± 106	—	−153 + 108
% with ≥ 15 letter gain	—	4/23 (16%)	—	5/25 (20%)
% with ≤ 15 letter loss	—	25/25 (100%)	—	25/25 (100%)

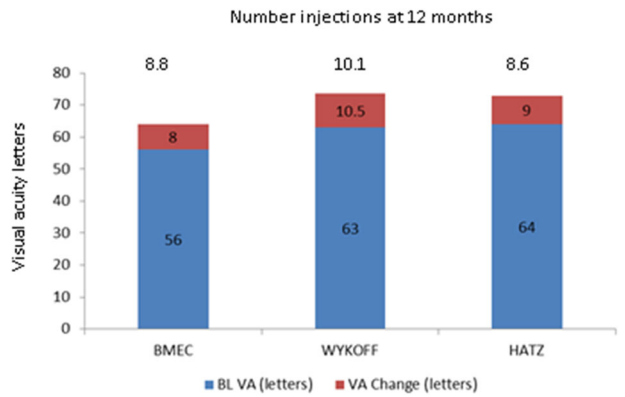

Fig. 1 [RF10]: Local results compared with those from RCTS

APPENDIX

Lucentis® (ranibizumab) ABBREVIATED UK PRESCRIBING INFORMATION

Please refer to the SmPC before prescribing Lucentis 10 mg/ml solution vial for injection, or Lucentis 10 mg/ml solution for injection in pre-filled syringe.

Presentations: A glass single-use vial containing 0.23 ml solution containing 2.3 mg of ranibizumab (10 mg/ml) and a pre-filled syringe containing 0.165 ml, equivalent to 1.65 mg ranibizumab (10 mg/ml).

Indications: The treatment in adults of neovascular (wet) age-related macular degeneration (AMD), the treatment of visual impairment due to choroidal neovascularisation (CNV), the treatment of visual impairment due to diabetic macular oedema (DMO), the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).

Administration and Dosage: Available as a single-use vial and a single dose pre-filled syringe, for intravitreal use only. Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections under aseptic conditions. The recommended dose is 0.5 mg (0.05 ml).

The interval between two doses injected into the same eye should be at least four weeks.

Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity i.e., no change in visual acuity or in other signs and symptoms of the disease under continued treatment. In patients with wet AMD, DMO and RVO, initially, three or more consecutive, monthly injections may be needed. Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity, as assessed by visual acuity and/or anatomical parameters.

If, in the physician's opinion, visual and anatomic parameters indicate that the patient is not benefiting from continued treatment, Lucentis should be discontinued.

Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g., optical coherence tomography or fluorescein angiography).

If patients are being treated according to a treat and extend regimen, once maximum visual acuity is achieved and/or there are no signs of disease activity, the treatment intervals can be extended stepwise until signs of disease activity or visual impairment recur. The treatment interval should be extended by no more than two weeks at a time for wet AMD and may be extended by up to one month at a time for DMO. For RVO, treatment intervals may also be gradually extended, however there are insufficient data to conclude on the length of these intervals. If disease activity recurs, the treatment interval should be shortened accordingly.

The treatment of visual impairment due to CNV should be determined individually per patient based on disease activity. Some patients may only need one injection during the first 12 months; others may need more frequent treatment, including a monthly injection. For CNV secondary to

pathologic myopia (PM), many patients may only need one or two injections during the first year.

Lucentis and laser photocoagulation in DMO and in macular oedema secondary to BRVO: There is some experience of Lucentis administered concomitantly with laser photocoagulation. When given on the same day, Lucentis should be administered at least 30 minutes after laser photocoagulation. Lucentis can be administered in patients who have received previous laser photocoagulation.

Lucentis and Visudyne photodynamic therapy in CNV secondary to PM: There is no experience of concomitant administration of Lucentis and Visudyne.

Before treatment, evaluate the patient's medical history for hypersensitivity..

Children and adolescents: Safety and efficacy in children and adolescents below 18 years of age have not been established. Limited data are available for adolescents aged 12 to 17 years with visual impairment due to CNV.

Elderly: No dose adjustment is required in the elderly. There is limited experience in patients older than 75 years with DMO.

Hepatic and renal impairment: Dose adjustment is not needed in these populations.

Contraindications: Hypersensitivity to the active substance or excipients. Patients with active or suspected ocular or periocular infections. Patients with active severe intraocular inflammation.

Special warnings and precautions for use: Lucentis is for intravitreal injection only. Intravitreal injections have been associated with endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract. Monitor during week following injection for infections. Patients should be instructed to report symptoms suggestive of any of the above without delay. Transient increases in intraocular pressure (IOP) within 1 h of injection and sustained IOP increases have been identified. Both IOP and perfusion of the optic nerve head should be monitored and managed appropriately. Limited data on bilateral use of Lucentis (including same-day administration) do not suggest an increased risk of systemic adverse events compared with unilateral treatment. There is a potential for immunogenicity with Lucentis which may be greater in subjects with DMO. Patients should report an increase in severity of intraocular inflammation. Lucentis should not be administered concurrently with other anti-VEGF agents (systemic or ocular). Withhold dose and do not resume treatment earlier than the next scheduled treatment in the event of the following: a decrease in best-corrected visual acuity (BCVA) of ≥30 letters compared with the last assessment of visual acuity; an intraocular pressure of ≥30 mmHg; a retinal break; a subretinal haemorrhage involving the centre of the fovea, or if the size of the haemorrhage is ≥50% of the total lesion area; performed or planned intraocular surgery within the previous or next 28 days. Risk factors associated with the development of a retinal pigment epithelial (RPE) tear after anti-VEGF therapy for wet AMD include a large and/or high pigment epithelial retinal detachment. When initiating Lucentis therapy, caution should be used in patients with these risk factors for RPE tears. Discontinue treatment in cases of rhegmatogenous retinal detachment or stage 3 or 4 macular holes.

There is only limited experience in the treatment of subjects with DMO due to type I diabetes. Lucentis has not been studied in patients who have previously received intravitreal injections, in patients with active systemic infections, proliferative diabetic retinopathy or in patients with concurrent eye conditions such as retinal detachment or macular hole. There is also no experience of treatment with Lucentis in diabetic patients with an HbA1c over 12% and uncontrolled hypertension. In PM patients there are no data on the use of Lucentis in patients with extrafoveal lesions and only limited data on its use in those who have had previous unsuccessful therapy with verteporfin photodynamic therapy. Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors.

There are limited data on safety in the treatment of DMO, macular oedema due to RVO and CNV secondary to PM patients with prior history of stroke or transient ischaemic attacks. Caution should be exercised when treating such patients. There are insufficient data to conclude on the effect of Lucentis in patients with RVO presenting irreversible ischaemic visual function loss.

Interactions: No formal interaction studies have been performed. In DMO and BRVO adjunctive use of laser therapy and Lucentis was not associated with any new ocular or non-ocular safety findings. In clinical studies for the treatment of visual impairment due to DMO, the outcome with regard to visual acuity or central retinal subfield thickness (CSFT) in patients treated with Lucentis was not affected by concomitant treatment with thiazolidinediones.

Pregnancy and lactation: Women of childbearing potential should use effective contraception during treatment. No clinical data on exposed pregnancies are available. Ranibizumab should not be used during pregnancy unless the expected benefit outweighs the potential risk to the foetus. For women who wish to become pregnant and have been treated with ranibizumab, it is recommended to wait at least three months after the last dose of ranibizumab before conceiving. Breast-feeding is not recommended during the use of Lucentis

Driving and using machines: The treatment procedure may induce temporary visual disturbances and patients who experience these signs must not drive or use machines until these disturbances subside.

Undesirable effects: Most adverse events are related to the injection procedure. Serious adverse events reported include endophthalmitis, blindness, retinal detachment, retinal tear and iatrogenic traumatic cataract. The safety data below include adverse events experienced following the use of Lucentis in the entire clinical trial population. Those marked * were only seen in the DMO population. Very common: Intraocular pressure increased, headache, vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, eye pain, vitreous floaters, conjunctival haemorrhage, eye irritation, foreign body sensation in eyes, lacrimation increased, blepharitis, dry eye, ocular hyperaemia, eye pruritus, arthralgia, nasopharyngitis. Common: Urinary tract infection*, anaemia, retinal degeneration, retinal disorder, retinal detachment, retinal tear, detachment of the retinal pigment epithelium, retinal pigment epithelium tear, visual acuity reduced, vitreous haemorrhage, vitreous disorder, uveitis, iritis, iridocyclitis, cataract, cataract subcapsular, posterior capsule opacification, punctuate keratitis, corneal abrasion, anterior chamber flare, vision blurred, injection site haemorrhage, eye haemorrhage, conjunctivitis, conjunctivitis allergic, eye discharge, photopsia, photophobia, ocular discomfort, eyelid oedema, eyelid pain, conjunctival hyperaemia, cough, nausea, allergic reactions, hypersensitivity, and anxiety.

Product-class-related adverse reactions: There is a theoretical risk of arterial thromboembolic events, including stroke and myocardial infarction, following intravitreal use of VEGF inhibitors. A low incidence rate of arterial thromboembolic events was observed in the Lucentis clinical trials in patients with AMD, DMO, RVO and PM and there were no major differences between the groups treated with ranibizumab compared to control.

Please refer to the SmPC for full listing of all undesirable effects.

For UK: Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard**. Adverse events should also be reported to Novartis Pharmaceuticals UK Ltd on (01276) 698370 or** medinfo.uk@novartis.com.

Legal category: POM, UK Basic NHS cost: £551 Marketing authorisation number: single dose vial injection kit EU/1/06/374/001, single dose vial only pack EU/1/06/374/002, single dose vial and filter needle pack EU/1/06/374/003, single dose pre-filled syringe EU/1/06/374/003

Marketing authorisation holder: Novartis Europharm Limited, Frimley Business Park, Camberley, GU16 7SR, United Kingdom. Full prescribing information, including SmPC, is available from: Novartis Pharmaceuticals, Frimley Business Park, Frimley, Camberley, Surrey, GU16 7SR. Telephone: 01276 692255. Fax: 01276 692508.

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