EURETINA
European Society of Retina Specialists

EURETINA
EDUCATION
PLATFORM

THE GREAT FLUID DEBATE

Reviewing Treatment Outcome Goals for the Wet AMD Patient

Independent medical education supported by Novartis & ZEISS

Baseline Trends in Wet AMD Treatment

Univ.- Prof. Dr. Frank G. Holz, FEBO, FARVO

Department of Ophthalmology, University of Bonn, Bonn, Germany, frank.holz@ukbonn.de

"The Great Fluid Debate" relates to the management of patients with neovascular age-related macular degeneration (wet AMD). The Interim 2019 EURETINA Clinical Trends Survey was designed to collect information on current practice trends and standard of care in treatment of wet AMD, and to identify unmet needs. It included 33 questions, and almost 300 EURETINA delegates participated in answering the online survey.

Practice Patterns

Practice patterns among the respondents are quite varied as shown by a widespread number of anti-VEGF injections performed in their practices weekly. Importantly, 27% of respondents perform over 30 anti-VEGF injections per week.

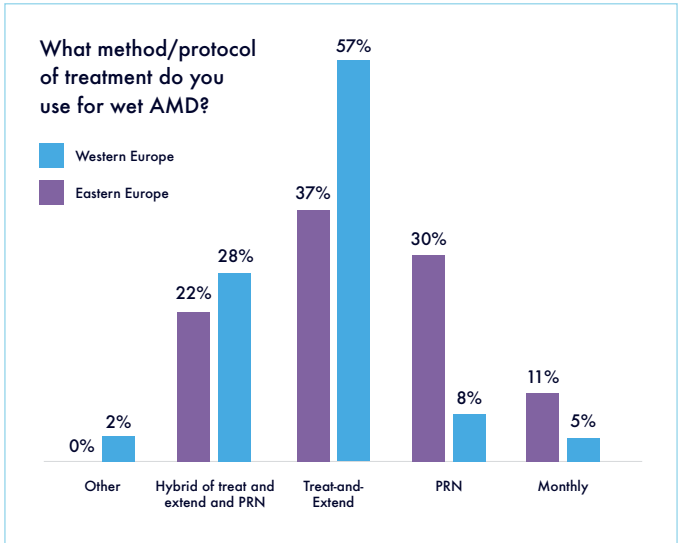
Patient Adherence

Patient adherence is key to the success of treatment. Not returning for monitoring or treatment can cause patients to irreversibly lose visual function. When asked what percentage of patients who require regular anti-VEGF injections are adherent with their treatments' timeframes, 32% reported that less than 60% are adherent. This is an alarming number, so we need to think about strategic approaches moving forward to improve it. Emerging therapies will also help address this issue.

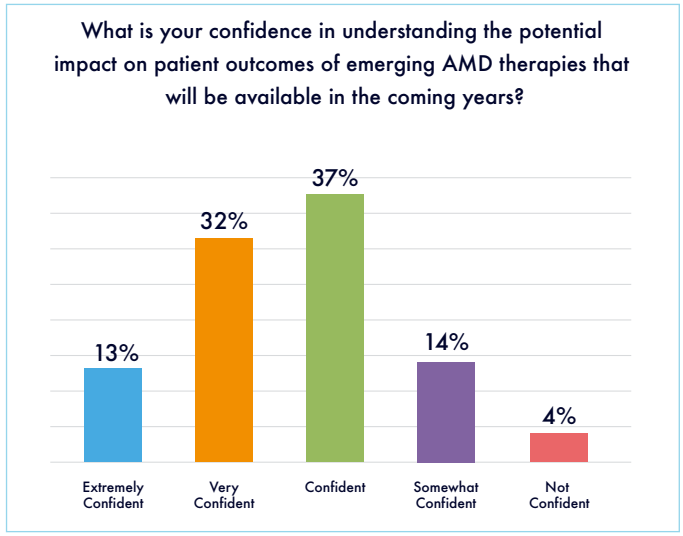
Treatment Approach

Different approaches are used in terms of when to have a patient return for anti-VEGF injections. Some may inject monthly, others use an as needed (PRN) regimen, and others a treat-and-extend approach. There are also hybrid forms combining the latter two. And there may not be uniform definitions on re-treatment criteria.

In answering what the preferred treatment regimen is for patients with wet AMD, there was a split between Western and Eastern Europe. The vast majority of Western European respondents, 85%, preferred a treat-and-extend, or a hybrid PRN/treat-and-extend approach for neovascular AMD treatment. For Eastern Europeans only 59% prefer that same management. There is not enough data to draw conclusions, but it's possible there are country-specific differences in how ophthalmologists approach their patients. Different reimbursement schemes may also play a role.



The Interim 2019 EURETINA Clinical Trends Survey Outcomes: Wet AMD treatment regimens. It was found that 85% of Western European delegates and 59% of Eastern European delegates prefer treat-and-extend or a hybrid of this approach.



The Interim 2019 EURETINA Clinical Trends Survey Outcomes: Emerging treatments. Only 44% are extremely or very confident in their understanding of emerging AMD therapies.

> ***"Patient adherence is key to the success of treatment. Not returning for monitoring or treatment can cause patients to irreversibly lose visual function."***

Emerging Therapies

Emerging therapies will address compliance and adherence, as well as hopefully improving efficacy. When asked about their level of confidence in understanding the potential impact of emerging AMD therapies on patient outcomes only 44% felt that they are very confident in having ideas of how new emerging therapies differ and distinguish from what is available today.

Keys to Accurately and Consistently Diagnosing Fluid Levels With Multimodal Imaging

Prof. Dr. Dr. Sebastian Wolf

Department of Ophthalmology, Inselspital University of Bern, Switzerland, sebastian.wolf@insel.ch

The Interim 2019 EURETINA Clinical Trends Survey shows that the majority of respondents are confident using multimodal imaging. In the survey, delegates were asked what imaging technique they use at the time of diagnosis for wet AMD, and 84% of respondents said they use multiple imaging techniques. The average respondent uses two techniques for multimodal imaging.

Why not use Multimodal Imaging?

For those not doing multimodal imaging, the most frequent reason (47%) is that it's not economically viable for their practice. So the hesitation isn't about using more technology; it is financial.

The survey asked respondents about their belief on the current value of OCT angiography (OCTA), a new technique that not everyone has access to. But 68% of respondents are using it or intend to use it.

What is Multimodal Imaging?

Multimodal imaging is the use of more than one technological system to acquire images, concurrently or in a short period of time, that complement one another for the purpose of diagnosis, prognostication, management, and monitoring of disease.

There are some problems with this. You get a lot of data, which is all in different silos and may be difficult to organise. There is data from fundus imaging and OCT data, and more if you include OCTA. It can become an overload of disconnected data, which then must be manually connected.

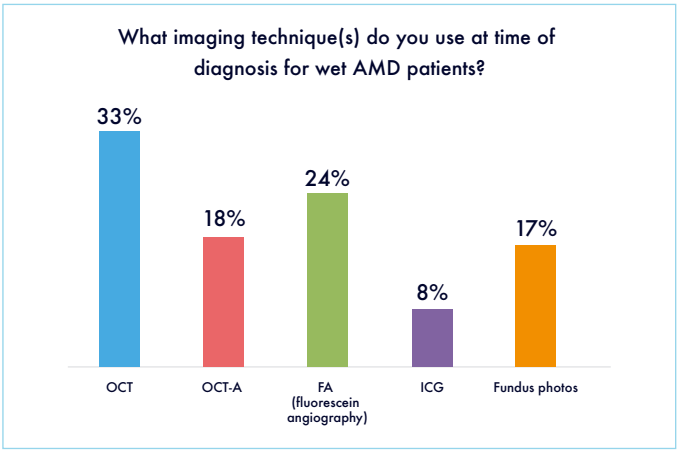
Using multiple imaging modalities with frequent imaging episodes creates a lot of data over time. More data creates larger file sizes that take longer to access and require more storage space.

Image technology has increased dramatically. Fundus photography was used in the 1920s, but it took more than another 30 years to have fluorescein angiography, and then another 30 to 50 years to have something new. But over the last few years there have been many new technologies, including OCTA, which was commercialised in 2016. And a lot of practices are using it, creating an explosion of data.

Swept Source OCT

Today OCT is the most important decision tool for retinal diseases. It provides 3D images, is non-invasive, very fast, reproducible, easy to do, and relatively easy to interpret. It's critical for confirmation of diagnosis, determining the best therapy, and to assess anatomic response to therapy, and potentially even for diagnosis. For patients with AMD, some doctors now only use OCT and don't see a need for fundus autofluorescence (FA).

> ***"In clinical practice, it's useful to combine images from all the different modalities and different time points into the same system."***



The Interim 2019 EURETINA Clinical Trends Survey outcomes: Multimodal imaging. It was found that 84% of delegates use multiple imaging techniques to diagnose wet AMD. The average delegate uses two techniques for multimodal imaging.

Swept Source OCT (SSOCT) has a scanning range of 12 mm to 16 mm scan lengths. There is no sensitivity roll off so you can image vitreous and the choroid simultaneously. With a longer wavelength there is better penetration of the tissue, and there is less trade-off between imaging size and resolution.

On the negative side, SSOCT is quite a bit more expensive than previous systems. There is less axial resolution, and it has a little bit worse signal-to-noise ratio and more motion artifact. Also, there are no normative databases yet because there are not many of them being used.

OCT Angiography

The principle of OCTA is that if stationary tissue is imaged, there are time-independent images. But if there are moving particles, there is a decorrelation signal, and from this we can calculate the vessels, which helps determine whether or not the eye shows neovascularization.

OCTA diagnostic instruments, such as the Zeiss Angioplex, have several clinical advantages. It's a minimal cost to use, once you have the instruments you don't need to use dye. But you don't see leakage in these pathologies.

OCTA is most helpful in diagnosing type 1 choroidal neovascularization (CNV). In these patients OCTA shows in many cases the vascular structure of the CNV and proves the presence of new vessels. However, the treatment decision is usually not based on OCTA but on signs of CNV activity in the structural OCT. These signs are sub-retinal pigment epithelium (RPE), sub-retinal (SRF), or intraretinal fluid (IRF) accumulation. We see regularly patients with the double layer sign in structural OCT without any fluid accumulations but a vascular network on OCTA. These patients we usually follow closely without treatment.

Fundus Autofluorescence

FA can be used to observe both central and peripheral retinal health by evaluating the fluorescence of lipofuscin produced by photoreceptors

and seems to be helpful in the diagnosis of hereditary diseases. FA images can be used to look at the retinal thickness, which can be helpful in the diagnosis of geographic atrophy and for follow-up, especially in diabetic macular edema where it's useful to follow the thickness and the changes in thickness. A decrease of retinal thickness could indicate a photoreceptor loss.

Autofluorescence imaging is recommended in AMD patients to monitor the presence of geographic atrophy. Additionally, autofluorescence imaging is very helpful to differentiate between atrophy secondary to AMD and atrophy in late onset Stargardt disease.

Integrating Data With Imaging

In clinical practice, it's useful to combine images from all the different modalities and different time points into the same system. They can then be reviewed together, which permits better visualisation and assists in decision-making. Artificial intelligence (AI) may play a role with this in the future.

Multimodal imaging is used to detect biomarkers of disease. There are predictive lesions like hyperreflective foci, pseudodrusen, nascent geographic atrophy, sub-RPE hyperreflective columns, or reflective drusen and sub-retinal structures.

AI may be able to help detect abnormalities and to assist with diagnosis, classification, prediction, prognosis, and therapy optimisation. This will enhance our ability to provide care.

All Retinal Fluid Should Be Eliminated to Maximise Outcomes for Wet AMD Patients

Martin S. Zinkernagel, MD, PhD

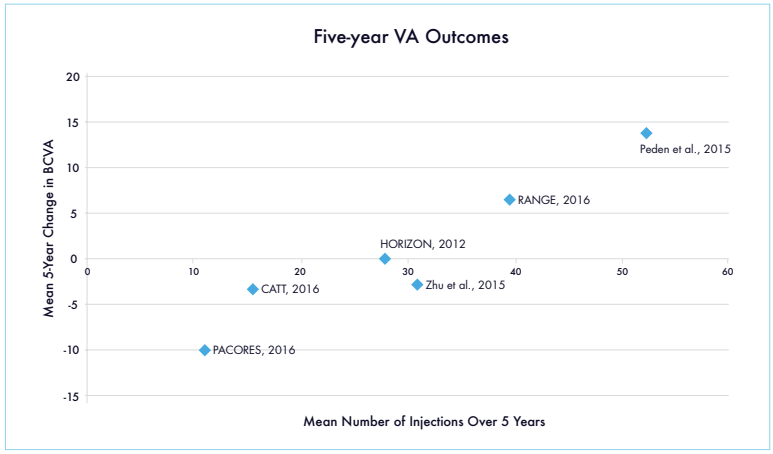
Department of Ophthalmology, Inselspital University of Bern, Switzerland, martin.zinkernagel@insel.ch

Data from large randomised clinical trials (RCTs) as well as clinical experience show that both SRF and IRF are associated with disease activity.

Therefore, intensive intravitreal treatment with anti-VEGF agents is needed to achieve best functional outcomes.

Published Guidelines

This is also reflected by guidelines on the treatment of wet AMD such as the 2014 published EURETINA Guidelines.[1] These guidelines recommend that whenever any evidence of fluid is noted by retinal imaging, an injection should be given to secure the optimal results in vision outcome. In addition, more and more data on long-term outcomes after anti-VEGF treatment has become available, supporting the fact that intensive treatment offers the best outcomes. The image below shows results from a meta-analysis of long term outcomes with different treatment regimens[2] essentially showing that the number of injections correlates with visual acuity gains at five years of treatment.



Five-year visual acuity outcomes vs. injection frequency in wet AMD.

Type of Fluid Matters

Whereas the negative effects of persisting IRF are undisputed, there is more controversy about persisting SRF or sub-RPE fluid. Almost all studies have shown IRF to be a poor prognostic factor for visual function and that it needs to be treated aggressively until maximum resolution is achieved.

Multiple studies show that stable SRF may be associated with better visual outcomes, but this has only been shown for the first two years of treatment.[3-6] However, we don't know what the functional outcome will be if someone has SRF for several years.

OCT Imaging

OCT images of patients with SRF often show that the outer retinal layers are less disrupted than in patients with IRF. However, we do not have data about the effects of persisting SRF over the course of many years. Clinical experience from patients with central serous chorioretinopathy would suggest that this would lead to photoreceptor degeneration in the end.

Questions About SRF

Something to consider is that the presence of SRF may positively influence the need for retreatment, so these patients may potentially get more frequent injections. As these patients receive more injections, they do a lot better and are able to maintain the initial visual acuity gains.

Another thing to remember is that residual SRF may not always represent ongoing neovascular activity. It may instead be dysfunction of the retinal pigment epithelium leading to SRF accumulation, much like central serous chorioretinopathy.

In addition, there are still many open questions such as how much SRF we can tolerate. For example, what would be the exact amount of fluid we can tolerate?

Conclusions

Current knowledge from studies, but also from clinical experience, suggests that residual fluid is associated with poorer visual outcomes. The exact role of SRF is still not fully elucidated and needs to be confirmed in further clinical trials. However, as SRF is a sign of persisting activity I would recommend to treat until maximal resolution is achieved.

Based on current clinical data and clinical practicability, outcomes are best if all fluid is treated rigorously when using protocols other than fixed dosing, or in other words, "if in doubt, inject the fluid out."

References

1. Schmidt-Erfurth U, Chong V, Loewenstein A, et al. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). *The British journal of ophthalmology*. 2014;98(9):1144-1167.
2. Qin VL, Young J, Silva FQ, Conti FF, Singh RP. Outcomes of patients with exudative age-related macular degeneration treated with antivascular endothelial growth factor therapy for three or more years: A Review of current outcomes. *Retina* (Philadelphia, Pa). 2018;38(8):1500-1508.
3. Schmidt-Erfurth U, Eldem B, Guymer R, et al. Efficacy and safety of monthly versus quarterly ranibizumab treatment in neovascular age-related macular degeneration: the EXCITE study. *Ophthalmology*. 2011;118(5):831-839.
4. Wickremasinghe SS, Janakan V, Sandhu SS, Amirul-Islam FM, Abedi F, Guymer RH. Implication of recurrent or retained fluid on optical coherence tomography for visual acuity during active treatment of neovascular age-related macular degeneration with a treat and extend protocol. *Retina* (Philadelphia, Pa). 2016;36(7):1331-1339.
5. Sulzbacher F, Roberts P, Munk MR, et al. Relationship of retinal morphology and retinal sensitivity in the treatment of neovascular age-related macular degeneration using aflibercept. *Investigative ophthalmology & visual science*. 2014;56(2):1158-1167.
6. Guymer RH, Markey CM, McAllister IL, Gillies MC, Hunyor AP, Arnold JJ. Tolerating Subretinal Fluid in Neovascular Age-Related Macular Degeneration Treated with Ranibizumab Using a Treat-and-Extend Regimen: FLUID Study 24-Month Results. *Ophthalmology*. 2019;126(5):723-734.

AMD Patients Can Tolerate a Small Amount of SRF With no Impact on Visual Outcome, and it May Be Helpful in Some Patients

Ramin Tadayoni, MD, PhD

Department of Ophthalmology, University of Paris – Lariboisière, Saint Louis & Cochin Hospitals, France, ramin.tadayoni@aphp.fr

The argument of needing to remove all fluid is very extreme. Let's look at the other side of the argument, using real data.

The Interim 2019 EURETINA Clinical Trends Survey shows the usual mix of responses for fluid threshold goals. Leakage is the hallmark of exudative AMD, but are all fluids the same? And should fluid be handled the same in practice as in testing, which is not the real world?

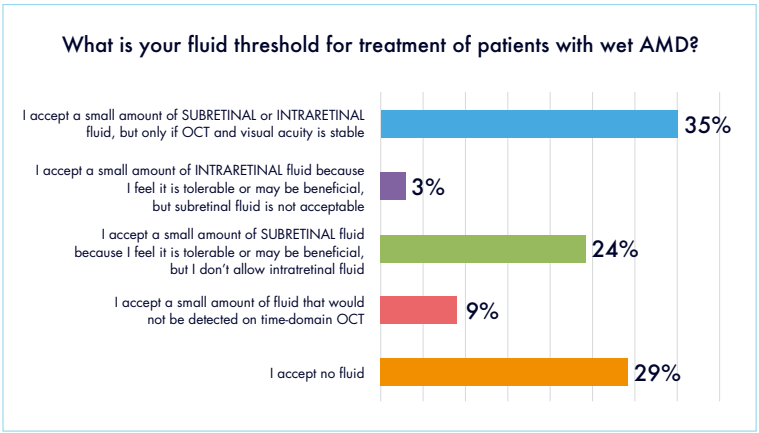
Are all Fluids the Same?

Patients with IRF prior to initial treatment don't do as well as those who have none. But patients who have SRF at baseline surprisingly do better in what I call the mid-term than patients who do not. This is true regardless of the anti-VEGF agent being used.

So, fluids are not the same, and SRF is correlated or associated with better visual acuity. This is not causality, just correlation: patients with SRF are often type 1 CNV and may have no atrophy, and the SRF involved in the centre of the fovea can cause low visual acuity that can resolve with SRF resorption for example.

During the Follow-up

A similar trend is found in patients having SRF during the procedure. Again here, patients who have IRF won't do as well as patients who don't. But those who have SRF during the study do better than those who don't. So, it's not just at baseline but later on too, again demonstrating the fluids are not the same.



The Interim 2019 EURETINA Clinical Trends Survey outcomes: Fluid thresholds. It was found that 71% of delegates do accept small amounts of fluid.

The FLUID Study[1]

The FLUID study looked at the treatment strategy of removing as much fluid as possible. Patients were randomised into the relaxed arm and the intense arm. Both used treat-and-extend regimens with 0.5 mg of ranibizumab. Patients in the relaxed arm were treated until resolution of IRF was achieved, or until there was less than 200 microns of SRF only at the centre of the fovea, and in the intense arm until complete resolution of IRF and SRF was achieved. The results showed that there

is no difference in the two groups.

The relaxed arm had a large number of injections, but the intense arm needed even more. The additional injections didn't change anything, and indeed all the patients in both arms received a fairly good treatment.

The EXCITE Study[2]

The EXCITE study compared monthly and quarterly injections of ranibizumab. It would be expected that results wouldn't be as good in the quarterly dosing group, and it's true that for IRF, a quarterly fixed regimen doesn't bring good results. But surprisingly, again, those who have SRF and get injections every three months do as well as those who have monthly injections.

So, in terms of strategy, SRF isn't the same as IRF, and a very super-relaxed treatment regimen brings the same result as monthly injections.

Reconsider Extreme Treatment

If you believe in removing all fluid, look at the CATT study,[3,4] where a third of patients, and in the FLUID study where 10% of patients even after numerous injections, still had SRF. You can't just keep injecting more and more. There are other reasons for this occurrence, as flat, irregular, pigment epithelial detachment (FIPED) or SRF at edges of pigment epithelial detachment, etc., and continuing injections in these patients won't make a difference.

In some cases, injecting too much could harm the CNV. That might seem desirable, but maybe not. In type I CNV there are some data suggesting that in the area of the CNV there is no atrophy, though there is atrophy in other places. The area under the CNV is said to be "protected." Perhaps this type of CNV has some protective effects that can be nurtured. Similarly to raising children, you don't let them do whatever they want, at some point you have to say, "a little bit is okay, but too much is not good."

According to the EURETINA survey, that's what is mostly done, because doctors have real patients, not theoretical ones. And 71% of respondents sometimes tolerate fluid in their patients, possibly due to treatment burden of a more extreme approach.

Conclusions

Having some SRF does not seem to be as detrimental as having IRF and may even correlate with good results. The protocols tried for extreme treatment to dry up all fluid don't do significantly better than more relaxed treatment.

Increasing the number of injections can impact the quality of life and treatment adherence of the patient. Some patients will not keep returning if the injections are too much of a burden.

The collective intelligence of doctors in daily practice is on this side of this debate, that a small amount of SRF can sometimes be tolerated in the AMD patient with no impact on their vision. It is only tolerated because doctors are pragmatic and not extremists. A future treatment that gets rid of all fluid without negative effects will be welcome as a solution that can make everyone happy.

References

1. Guymer RH, Markey CM, McAllister IL, Gillies MC, Hunyor AP, Arnold JJ. Tolerating Subretinal Fluid in Neovascular Age Related Macular Degeneration Treated with Ranibizumab Using a Treat-and-Extend Regimen: FLUID Study 24-Month Results. *Ophthalmology*. 2019;126(5):723-734.
2. Schmidt-Erfurth U, Eldem B, Guymer R, et al. Efficacy and safety of monthly versus quarterly ranibizumab treatment in neovascular age-related macular degeneration: the EXCITE study. *Ophthalmology*. 2011;118(5):831-839.
3. Martin DF, Maguire MG, Fine SL, et al; Comparison of Age-related macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age related macular degeneration: two-year results. *Ophthalmology*. 2012;119(7):1388-1398.
4. Maguire MG; Martin DF, Ying G, et al; Comparison of Age-related macular Degeneration Treatments Trials (CATT) Research Group. Five-year outcomes with anti-vascular endothelial growth factor treatment of neovascular age-related macular degeneration [published online ahead of print May 2, 2016]. *Ophthalmology*. 2016 Aug;123(8):1751-1761. doi: 10.1016/j.ophtha.2016.03.045. Epub 2016 May 2.

Recent OCT Fluid Analyses and Their Clinical Implications

Pravin U. Dugel, MD

Managing Partner, Retinal Consultants of Arizona, pdugel@gmail.com

When it's suggested that some patients do well with some fluid, it's important to remember that they're still being treated to try and get the fluid out. Nobody is leaving fluid behind on purpose.

Analysing Fluid That Remains

How can we analyse the fluid that doesn't dry up? One way is to analyse drugs and how well they eliminate fluid. The OCT is the most important objective biomarker used to decide to switch to a different drug, or determine whether to treat a patient. But how do we use the OCT to compare drugs?

We have historically compared drug A and drug B to determine which drug dries the patient faster. Or we have compared drug A and drug B, and see which drug dries more patients than the other. But those are no longer the only two comparison options.

> ***"...if a physician chooses to accept some fluid, it can be done only under the condition that the patient is continually followed up and treated as needed."***

A New Way of Analysing Fluid

There is a fascinating new method of analysing fluid, which is to compare two drugs and see which causes fewer fluctuations in central subfield thickness (CST), as seen on OCT. This was first done by Dr.

Usha Chakravarthy, who analysed the CATT and IVAN studies.[1] Information gained with this method may be very important.

Dr. Chakravarthy's group divided the patient population into four different quartiles – from those that didn't have very much fluctuation, up to those that had a lot of fluctuations. It should be emphasised that this was agnostic of the drug; they looked only at the fluctuations.

In a collaboration between physician investigators and Novartis, we then did the same analysis with the HAWK and HARRIER data.[2] Minimal fluctuations were used as the reference point. With fluctuations considered a dose, it was clearly seen, in a dose-dependent fashion, that the more fluctuations there are, the worse the vision. It's remarkable and absolutely consistent in all studies.

Confidence in the Method

When dose-dependent consistency is seen, it provides a lot of confidence. What provides even more confidence is that the results of this study look virtually identical to what the previous group showed with the CATT and IVAN data. We now have four studies done by two different groups that all show fluctuations in CST may be a new and very important way to look at OCT data, in terms of how it will impact vision.

Early Prediction

Very importantly, looking at fluctuations and separating them into quartiles to predict how a patient is going to do can be done as early as week eight. When following change in BCVA over time, separation was seen in the response of the quartiles at week eight, and the resulting plot lines never crossed through the end of follow-up.

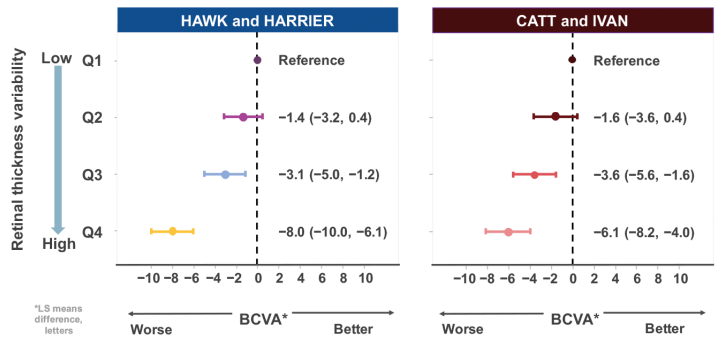
Thus, at that early point it will be possible to tell a patient they may need more injections with closer follow up because their fluctuations are greater and to tell another patient they may be able to have a slightly relaxed treatment regimen because their fluctuations are less.

Combine the Data

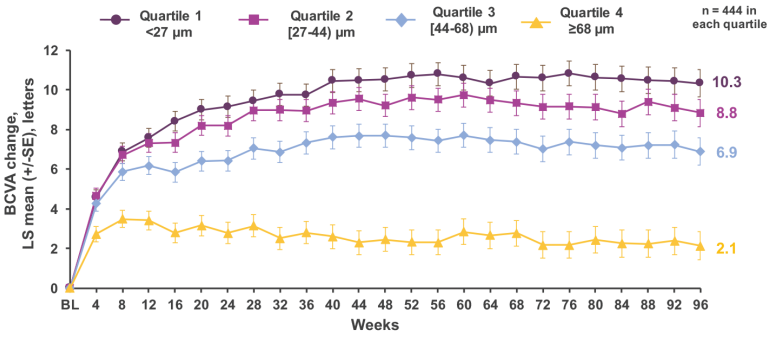
Fluctuations in CST are not in opposition with seeing fluid on OCT. The two go hand-in-hand. Separating the quartiles and looking at who had fluid, we saw that patients with more fluctuations also were more likely to have fluid, which makes sense. They were more difficult to treat. So there is a direct correlation between vision, fluid, the amount of fluid, and fluctuations in CST.

Conclusions

There are different ways to look at OCT data, and different analyses are being done to compare drugs, because it's important to have objective data. The objective data can include how quickly a drug dries the retina and also in how many patients it is effective for drying the retina. But a new third method, which may be equally or more impactful, is to look at what effect a drug has on fluctuations in CST, which may prove to be extremely meaningful for these patients.



Left panel: LS mean and SE estimates are based on an ANCOVA model with baseline BCVA, study treatment and CST variability quartile as fixed effect factors. This is combined data for brolucizumab and aflibercept. SD (CST) quartile, µm for H&H - Q1 <27; Q2 [27–44); Q3 [44–68); Q4 ≥68. Error bars represent 95% confidence intervals. Right panel: reproduced from Evans et al, "Associations between variation in retinal thickness and visual function", ARVO 2019 poster. BCVA, best-corrected visual acuity; CST, central subfield thickness; LS, least squares; Q, quartiles; SE, standard error; SD, standard deviation



Individual SD (CST) is for weeks 0 to 96. LS mean and SE estimates are based on an ANOVA model with baseline BCVA letters, study, treatment and CST variability quartile as fixed effect factors.
This is combined data for brolucizumab and aflibercept. BCVA, best-corrected visual acuity; BL, baseline; CST, central subfield thickness; LS, least squares; SE, standard error; SD, standard deviation

Images Courtesy of Novartis, reprinted with permission

References

1. Evans RN, Chakravarthy U, Reeves B. Associations between variation in retinal thickness and visual function. *ARVO* 2019 poster #3456.
2. Dugel PU, Koh A, Ogura Y, Jaffe GJ, Schmidt-Erfurth U, Brown DM, et al. HAWK and HARRIER: phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. *Ophthalmology.* 2019. https://doi.org/10.1016/j.ophtha.2019.04.017.

Some Stable SRF May Be Acceptable

Anat Loewenstein, MD, FARVO

Chair, Department of Ophthalmology, Tel Aviv Medical Center, Vice Dean, Faculty of Medicine, Tel Aviv University, anatl@tlvmc.gov.il

Prior to the "Great Fluid Debate" symposium, the audience response system (ARS) answers for fluid threshold in patients with wet AMD showed only 28% of respondents answered that a small amount of SRF is acceptable, but not IRF. This is surprising, because, while there is still a debate of whether or not SRF is important, there's almost a consensus that IRF is worse than SRF. I was also surprised that 7% accept small amounts of fluid on time-domain OCT, simply because I wouldn't think time-domain OCT would be used anymore. So even though 7% is not a lot, it's surprising that some still use this method. For the respondents thinking SRF is worse than IRF, 8% may seem like a small number, but it's larger than it should be, as this is not the common belief. And almost a third of respondents said they accept a small amount of either fluid if it remains stable, and if visual acuity is also stable, which is a widely held view.

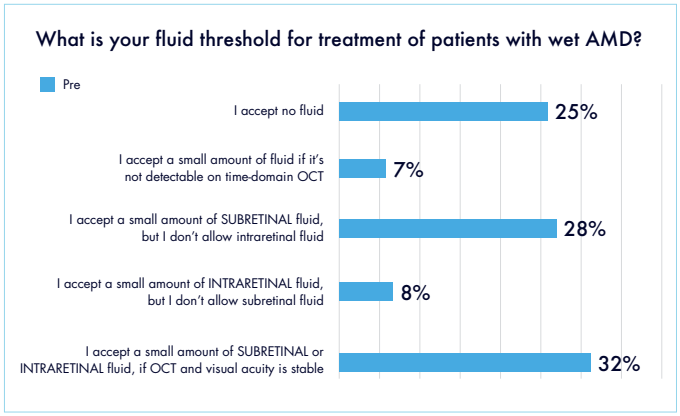
With regard to SRF, some believe the retina should be completely dry, and may move a patient to a drug they believe will make the retina drier, for example choosing brolucizumab over aflibercept based on trial results. Others think it's not necessary to continue treatment as long as visual acuity and fluid levels remain stable.

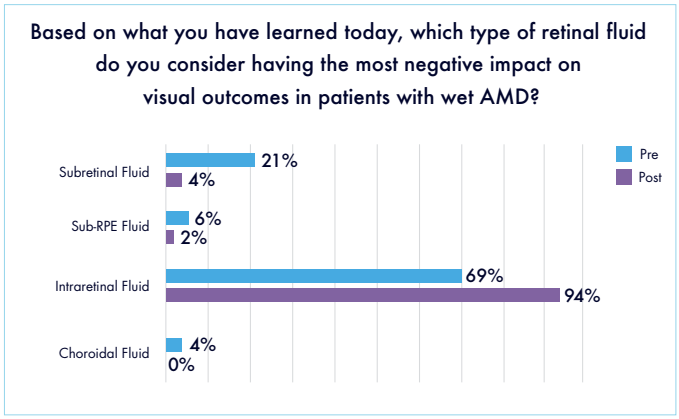
Very importantly, if a physician chooses to accept some fluid, it can be done only under the condition that the patient is continually followed up and treated as needed.

As I would expect, about two-thirds of respondents were very confident in their ability to diagnose wet AMD using multimodal imaging and then a little more after the symposium based on what they had learned. It makes sense that 20% to 30% would be only somewhat confident even after the symposium, because the process allows variability of interpretation, so they may not have complete confidence in the process. Physicians don't always diagnose the same as reading centres, or even the same as other physicians. This includes detecting activity of disease as well as existing AMD. And almost everyone plans on using multimodal imaging, which certainly is better than using a single imaging mode.

Following the programme, almost all respondents emphasise that IRF is more dangerous than SRF. About two-thirds thought so at first, and almost everyone after reflecting what was said in the programme.

Everyone wants to reduce fluid. The debate is, if you can't reduce it, and visual acuity is not declining, and the degree of SRF is stable, do you just observe, or perhaps look at another drug? If a patient is stable without treatment, the decision to choose only observation can reduce patient burden, side-effects, and cost. Of respondents in the survey, two-thirds continue to try to reduce fluid level to improve BCVA, and a third still believe that's not necessary. I think even for those in that group it's only true if visual acuity is stable and retinal fluid is not increasing and only with the patient being continuously followed up, and treated as necessary.





EURETINA
European Society of Retina Specialists

Supported by

NOVARTIS
Platinum

ZEISS
Silver