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HBM Healthcare Investments

Pressemitteilung

Zug, 14. Dezember 2012

Vielversprechender neuer Ansatz zur Behandlung der feuchten altersbedingten Makula-Degeneration

Mitte Juni veröffentlichte Ophthotech Corporation, ein privates Unternehmen im Portfolio von HBM Healthcare Investments, die Ergebnisse einer umfangreichen Phase 2b Studie mit 449 Patienten für einen Wirkstoff zur Behandlung der altersbedingten Makula-Degeneration (feuchte AMD). Die Studie zeigte bei Patienten, welche das von Ophthotech entwickelte Präparat Fovista™ in Kombination mit dem bekannten Medikament Lucentis® verabreicht erhielten, eine Verbesserung der Sehschärfe um 62% im Vergleich zu Patienten, welche mit Lucentis® alleine behandelt wurden.

Führende Ophthalmologen in den USA haben in den vergangenen Wochen die Studiendaten von Ophthotech analysiert und am Runden Tisch diskutiert. Das Ergebnis dieser Diskussion wurde kürzlich durch die Amerikanische Vereinigung von Retina Spezialisten im angefügten Papier veröffentlicht.

HBM Healthcare Investments hat seit 2007 insgesamt USD 16,5 Millionen in Ophthotech investiert und ist mit 15,7 % an der Gesellschaft beteiligt. Die Investition ist trotz der positiven Entwicklung unverändert zum Anschaffungspreis bewertet.

Für weitere Auskünfte wenden Sie sich bitte an Dr. Andreas Wicki, Tel.: +41 41 768 11 08, andreas.wicki@hbmhealthcare.com

Profil der HBM Healthcare Investments AG

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A SPECIAL SUPPLEMENT TO

RETINA TIMES

The Official Publication of the American Society of Retina Specialists

Anti-PDGF Therapy Offers New Approach to AMD Treatment

An Expert Roundtable Discussion Led by Pravin U. Dugel, MD

This supplement is sponsored by Ophthotech Corporation.

FALL 2012

J. Michael Jumper, MD
Editor-in-Chief

Can Combination Therapy Improve Wet-AMD Outcomes?

My mom (yes, I have her permission) has bilateral neovascular age-related macular degeneration (AMD). She was aware of her symptoms very early and began treatment with anti-VEGF therapy in 2007. Under the care of a good friend of mine, she remains 20/20-20/25 in each eye now, 5 years later.

To achieve this excellent outcome, she has required nonstop monthly bilateral injections. Fluorescein angiography done over this same time period demonstrates continued growth of the neovascular complex despite her macula remaining dry on OCT imaging. While near-miraculous for patients like my mom, anti-VEGF therapy is not a cure.

The hope of combination therapy to improve outcomes and/or decrease the treatment burden of wet AMD dates back to the time before anti-VEGF therapy, when steroids were used with photodynamic therapy (PDT). Since then, all conceivable combinations of available therapies have been tried; monotherapy remains the standard.

'Fovista represents one of many drugs in the pipeline that may become an invaluable tool in our ongoing battle with AMD.'

This supplement is a discussion of the results of a recently conducted phase 2b clinical trial comparing monotherapy with Lucentis (Genentech, South San Francisco, CA) with an inhibitor of platelet-derived growth factor (Fovista, Ophthotech Corporation, Princeton, NJ) in combination with Lucentis for subfoveal, neovascular AMD (www.clinicaltrials.gov, NCT01089517).

The findings, as described by the panel led by Pravin Dugel, MD, are interesting and give us hope that combination therapy may, one day, improve outcomes of wet AMD.

Ophthotech is the sponsor of this trial and also paid for the publication of this supplement. As such, this supplement does not represent an endorsement by the ASRS of this company or this product. I have agreed to publish this supplement because it is my opinion that the ASRS membership will find the data interesting.

These are exciting times in the field of vitreoretinal pharmacotherapy. Fovista represents one of many drugs in the pipeline that may become an invaluable tool in our ongoing battle with AMD. I hope *Retina Times* will be able to discuss other positive trial results soon.

Anti-PDGF + Anti-VEGF = Promising Approach to AMD Treatment

Financial Disclosures

Dr. Jumper – COVALENT MEDICAL, INC: Equity Owner, Stock; DUTCH OPHTHALMICS USA: Speaker, Honoraria.

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Phase 2b Trial Results Show Effectiveness of Combination Therapy

Discussion of results of "A Safety and Efficacy Study of E10030 (Anti-PDGF Pegylated Aptamer) Plus Lucentis for Neovascular Age-Related Macular Degeneration"[1]

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The introduction of anti-VEGF agents was a huge step forward in the treatment of neovascular AMD. Recently, a large phase 2b, 6-month study enrolling 449 patients investigated combination therapy with an inhibitor of platelet-derived growth factor-B (anti-PDGF-B, Fovista, formerly E10030, Ophthotech Corporation, Princeton, NJ) plus ranibizumab (Lucentis, Genentech, South San Francisco, CA) in patients with subfoveal neovascular AMD.[1]

Compared with ranibizumab monotherapy, treatment with Fovista 1.5 mg plus ranibizumab resulted in a 62% greater mean gain in visual acuity from baseline at 6 months, and there were no safety concerns.

PRAVIN DUGEL: The rationale for the use of Fovista with an anti-VEGF agent such as ranibizumab is well established in the general oncologic literature and may explain why anti-VEGF monotherapy requires routine maintenance injections, perhaps indefinitely.

Although VEGF is important in the early growth and maintenance of the neovascular complex, the vessels are covered with pericytes as the membrane matures. These specialized cells act as an armor that protects the neovascular complex from the effects of anti-VEGF agents. The recruitment, maturation, and survival of pericytes depend on PDGF-B, a cytokine released by tip cells in the growing neovascular membrane.

The biology of neovascular membrane development may explain why we see a plateau in the visual acuity improvement obtained with anti-VEGF monotherapy and enhanced efficacy with the addition of an anti-PDGF agent. Initiation of anti-VEGF monotherapy leads to eradication of tip cells—the only unprotected endothelial cells in the neovascular complex—and decreased exudation via its antipermeability effects. This leads to an improvement in visual acuity in the first 3 to 4 months.

Financial Disclosures

Drs. Dugel, Duker, Reichel, and Csaky are consultants for and have an equity position in Ophthotech Corporation. The rest have no financial relationship with Ophthotech. Complete financial disclosures for the roundtable participants are listed on page 6.

However, the neovascular membrane does not regress, but remains in suspension. Once anti-VEGF treatment stops, the tip cells begin to grow again, leading to continued choroidal neovascular membrane (CNVM) growth and leakage. By binding to and inhibiting the activity of PDGF-B, Fovista strips the pericytes from the CNVM, rendering it more sensitive to anti-VEGF therapy.

We have gathered a roundtable of internationally recognized thought leaders in retina to discuss the significance of the Fovista trial. Thank you all for your expertise.

'By binding to and inhibiting the activity of PDGF-B, Fovista strips the pericytes from the CNVM, rendering it more sensitive to anti-VEGF therapy.'

—Pravin U. Dugel, MD

All of you have seen the comprehensive data set pertaining to the efficacy, biomarker response, and safety results of this trial. Please give your initial reaction.

ELIAS REICHEL: The results are robust across the board—more visual acuity gainers and fewer losers relative to Lucentis, Eylea (Regeneron Pharmaceuticals, Inc, Tarrytown, NY), and Avastin (Genentech, South San Francisco, CA). Even if an ideal anti-VEGF monotherapy regimen is used, about 30% of patients will lose some vision—and here we are seeing a meaningful reduction of visual loss. There was a higher percentage of gainers, with 70% to over 100% relative vision improvement in certain categories. This is quite remarkable.

JAY DUKER: Until the Fovista phase 2b data, successful combination therapy for wet AMD was, from a practical perspective, just hypothetical. Combining corticosteroids and photodynamic therapy (PDT) with anti-VEGF agents has been studied fairly extensively but never caught on widely, as the addition of the steroid or PDT did not buy much more mileage.

Based on the Fovista/anti-VEGF phase 1 data, I thought the anti-PDGF/anti-VEGF combination therapy might be successful, but the visual results of this phase 2b Fovista combination trial greatly exceeded my expectations. I would never have thought this much visual benefit would be derived from targeting a second pathway. But it does make a lot of sense, as I study the PDGF-signaling mechanism.

MARCO ZARBIN: These are the most remarkable clinical data I have seen for the treatment of wet AMD in approximately 6 years. The anti-VEGF agents available currently are similar pharmacologically and do not seem to provide substantial visual improvement over monthly ranibizumab injections. The results of treatment involving Fovista plus ranibizumab demonstrate the power of combination therapy—the synergistic effect when combining 2 drugs with different mechanisms of action to attack a disease process.

The outcome of fundamental importance in the phase 2b Fovista trial is visual benefit. The phase 2b data of Fovista in combination with anti-VEGF are essentially like phase 3 data because of the large sample size of the randomized study. These data show true, substantial improvement over ranibizumab. Not only is combination therapy going to make the patient see better, but it could change the logistical burden and cost of treatment.

The other interesting aspect of this therapy is that physicians will be able to combine this drug with the anti-VEGF agent of their choice. You don't have to persuade patients or their physicians to use bevacizumab or ranibizumab or aflibercept.

'Anti-PDGF/VEGF combination clearly changes the underlying biology of the disease. If the phase 3 data hold up, combination therapy will become the standard of care, replacing the monotherapeutic anti-VEGF approach.'

—Karl G. Csaky, MD, PhD

KARL CSAKY: The vision data are very impressive. I don't think any of us thought we could do better than Lucentis. In the phase 1 study, we saw hints that anti-PDGF could change the equation. With this recent data, we are changing something fundamental in the biology of the disease when we add the anti-PDGF aptamer—if the data hold up in the phase 3 trial.

'It is likely ... that our current biomarkers ... are inadequate for this combined therapy.'

—Jay S. Duker, MD

We have come to realize that none of the 3 anti-VEGF agents—Lucentis, Eylea, or Avastin—is the final solution for the treatment of wet AMD. The results of the recent Seven-Up Study of ANCHOR/MARINA subjects[2] have revealed that after 7 years, more than one-third of wet-AMD patients treated continually with anti-VEGFs demonstrated vision of 20/200 or worse. Hence, the long-term benefit of anti-VEGF monotherapy is not substantial. By treating only the fluid and leakage, we are not fundamentally addressing the biology of the disease.

Anti-PDGF/VEGF combination clearly changes the underlying biology of the disease. If the phase 3 data hold up, combination therapy will become the standard of care, replacing the monotherapeutic anti-VEGF approach.

DAVID BOYER: The entirety of the data is very impressive; no subgroup drove this outstanding visual outcome. In this marketplace, in treating wet AMD, I think everybody would agree that one drug is not enough to give the optimal outcome. Fovista makes biologic sense; it definitely shows clinical improvement in overall vision and 3-line gain, and it seems consistent with the biologic basis of efficacy.

Relative vision improvement of approximately 62% is impressive. This phase 2b Fovista trial is the largest I have seen and there is no room for guessing. Examining the totality of data leaves no doubt that this improvement is real.

Fovista could be an adjunct to every anti-VEGF agent, and that potential for choice is very important. I foresee tremendous excitement among physicians for an adjunctive drug to improve the results of anti-VEGF

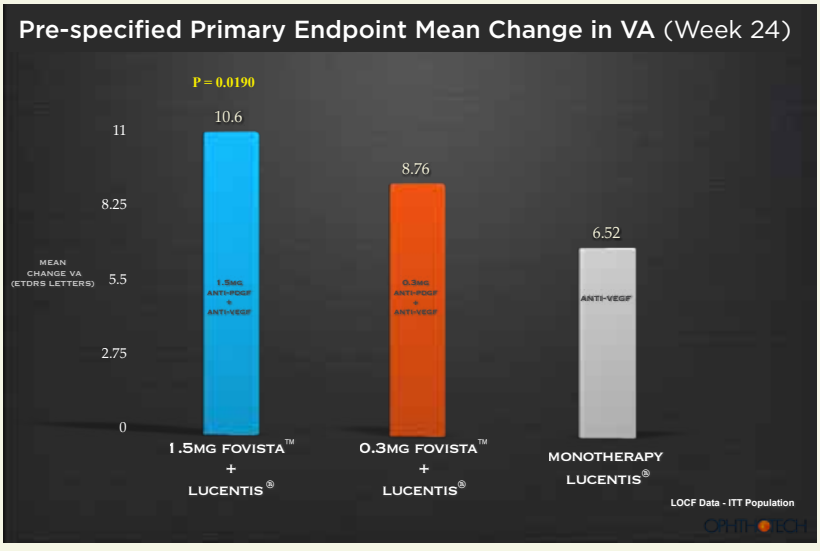

FIGURE 1

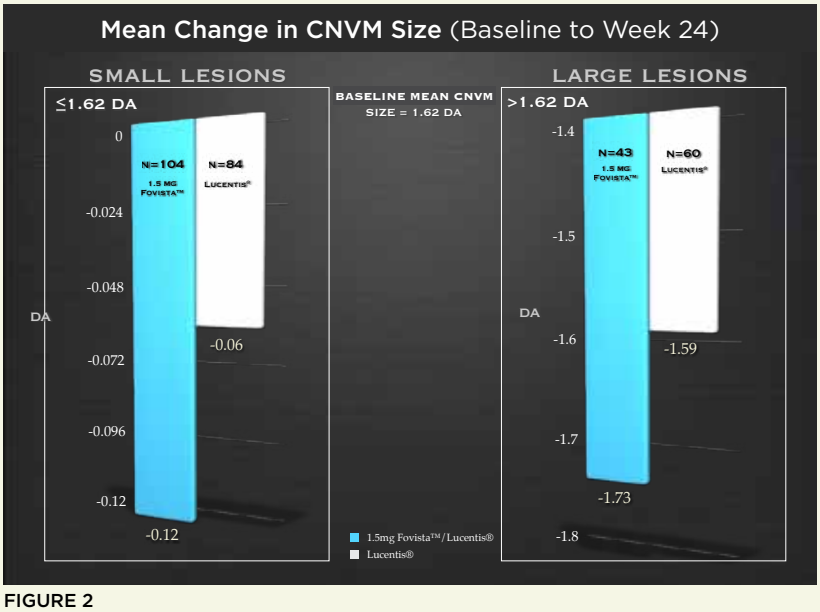

FIGURE 2

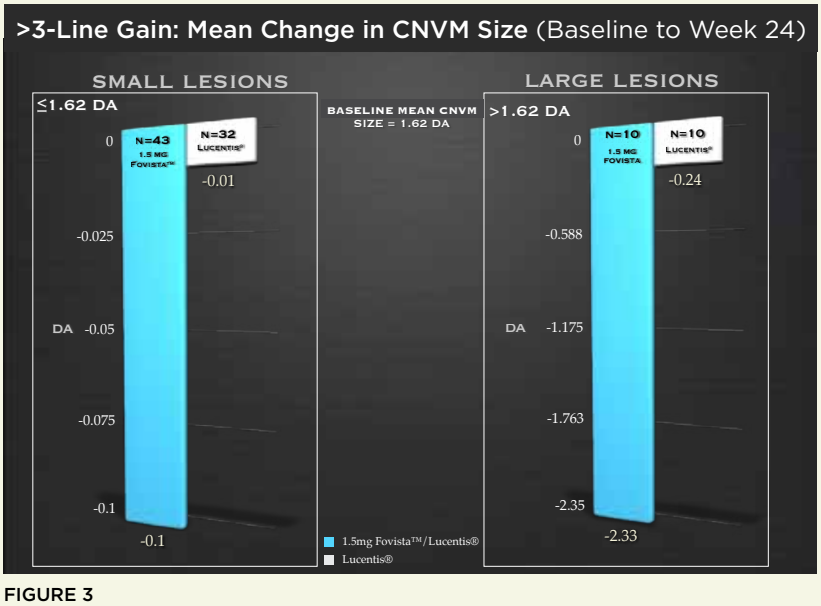

FIGURE 3

The Fovista combination group shows a direct and predictable dose-response in regard to vision improvement and reduction in lesion size. **FIGURE 1** shows the 62% improvement in efficacy with combination (1.5mg Fovista and Lucentis) treatment vs Lucentis monotherapy. **FIGURE 2** shows CNVM regression that correlates with baseline lesion size, ie, a larger CNVM would be expected to have a larger regression than a smaller CNVM. The results are as expected. **FIGURE 3** shows a direct correlation between vision improvement and lesion regression in large and small lesions. Neovascular AMD is a variable disease. Despite this, the direction of the results in vision improvement correlating with lesion regression is remarkably consistent.

monotherapy. I think there is significant flexibility for the Phase 3 trial design, as the trial can be performed with any anti-VEGF agent including Avastin.

PRAVIN DUGEL: Although the Fovista trial was a 6-month, phase 2 study, it was the largest phase 2 trial in retina, with 449 patients. At the 6-month mark, the visual acuity improvement curves were diverging. Every subgroup analysis consistently showed the superiority of combination treatment. In fact, a relative benefit of 25% over Lucentis monotherapy was attained in patients who gained 3 or more lines of vision, with 69% and 178% relative benefit in patients gaining 4 or more and 5 or more lines of vision, respectively.

'The results of treatment involving Fovista plus ranibizumab demonstrate the power of combination therapy—the synergistic effect when combining 2drugs with different mechanisms of action to attack a disease process ...'

—Marco A. Zarbin, MD, PhD

Let's now discuss the control arm—Lucentis administered monthly. Patients receiving the combination of Fovista (1.5 mg) and Lucentis gained a mean of 10.6 letters of vision on the ETDRS standardized chart at 24 weeks, compared with 6.5 letters for patients receiving Lucentis monotherapy ($P = .019$).

Did the control arm underperform?

JAY DUKER: I see no evidence that the Lucentis group underperformed. Six-letter improvement is in the ballpark of what we have seen at 6 months in several other anti-VEGF wet-AMD trials that enrolled all lesion types. Given the study design, selection bias should not have been an issue. Randomization and the large sample size of this study would negate any demographic biases between the control and the study groups.

KARL CSAKY: One should be very skeptical of cross-trial comparisons. That is the reason the FDA will not accept any cross-trial comparisons in the evaluation of a new therapy for neovascular AMD. In the VIEW 1/VIEW 2 trials, there were dramatically different results for supposedly identical patient recruitment characteristics: for example, recall the variability (mean vision = 10.9 vs 7.6) between the 2 mg q 4-week arms in the 2 trials. The only way to identify a true difference between 2 treatment modalities is in a direct head-to-head comparison in a large trial.

This phase 2b anti-PDGF combination trial with a large sample size and adequate follow-up assures me of the reliability of the data. The prospective nature and randomization of the phase 2b trial provide additional reassurance. For example, randomization equalizes all baseline variables and unknowns. It balances all the key variables—one of the main advantages of a large randomized trial. But one should never do cross-trial comparisons.

MARCO ZARBIN: Given the randomization and with no inherent differences between the starting population and the other group, the data are quite convincing. I do not believe Lucentis underperformed.

'This phase 2b anti-PDGF combination trial with a large sample size and adequate follow-up assures me of the reliability of the data.'

—Karl Csaky, MD, PhD

PRAVIN DUGEL: The Lucentis trials—ANCHOR, MARINA, PIER, PrONTO, CATT, IVAN, HARBOR—showed variable results. In the largest neovascular AMD study ever conducted, there was a 3.3-letter difference in the 2 mg q 8-week arm in the VIEW I and VIEW 2 trials. In the MARINA trial, 5% in the sham group (with no treatment) gained 3 or more lines of vision, while 31% in the Lucentis monthly group lost vision. This highlights the variability of the disease itself, influenced by intrinsic and extrinsic factors that can be controlled only by an adequate, randomized patient population.

The 6.5-letter gain in 6 months in this trial is consistent with the 6-month vision gain in many other trials with a monotherapy anti-VEGF regimen: MARINA ~6.0, CATT ~6.6, VIEW1 ~6.7, IVAN ~6.0 letters.

Let's discuss the role of biomarkers in managing patients if the phase 2b trial data of Fovista/anti-VEGF combination are confirmed in phase 3 trials. You all have seen the entire anatomic data. How will they help with managing wet-AMD patients?

GLENN JAFFE: There is increasing reliance on OCT in clinical practice and in clinical trials. On OCT, in eyes with neovascular AMD, we often see subretinal highly reflective material (SHRM)—an important component of the CNVM tissue under the retina. Although SHRM typically includes CNVM, by OCT it cannot be differentiated from admixed fibrous elements and blood. Regardless, SHRM's thickness appears to correlate with visual function. Therefore it is reasonable to hypothesize that if a drug caused reduced SHRM, visual improvement could ensue.

The presence or absence of SHRM was determined in the Fovista phase 2b study. Based on masked reading center assessment, SHRM resolution correlated with improved visual acuity, particularly in eyes that gained 3 lines of visual acuity.

Quantitative measurement of SHRM supported the results of the qualitative assessment and correlated with visual benefit. Therefore, adding Fovista to Lucentis, particularly in the high-dose (Fovista 1.5 mg) group, resulted in greater reduction of SHRM thickness and improved visual acuity.

'The outcome of fundamental importance in the phase 2b Fovista trial is visual benefit.'

—Marco A. Zarbin, MD, PhD

In approximately 50% of patients, there was complete absence of SHRM in the high-dose Fovista/Lucentis combination group, whereas approximately 90% of patients had SHRM at baseline. OCT methods to evaluate CNVM tissue—not just retinal thickness and fluid, especially given improving OCT technology—will likely play a greater role in future drug therapy treatment decisions.

JAY DUKER: When anti-VEGF therapy first became available, we all thought its beneficial effect was anti-neovascular based on the mechanism of action, ie, use of the medications would cause involution of the neovascular complex. We also thought that fluorescein angiography (FA) would have been a useful adjunct to monitor this effect. However, we rarely use FA in managing AMD patients, based on our clinical experience with anti-VEGF therapy.

'In eyes that showed the most visual improvement after being treated with Fovista and Lucentis, there was a trend for [highly reflective] spots to go away.'

—Elias Reichel, MD

The major beneficial effect of the anti-VEGFs is a reduction in vascular permeability. In real clinical practice, the majority of retina specialists individualize therapy using either a treat-and-extend or a PRN protocol. And the major ancillary test that guides our individualized therapy is OCT, not FA.

For anti-PDGF combination, we will likely need another biomarker if we choose individualized therapy. Is the visual improvement we are seeing in phase 2b Fovista based on fluid resorption, CNVM complex involution, fibrin dissolution, fibrosis reduction, or a combination of all of these?

I doubt FA will be quantifiable enough to guide us. It is incumbent on us to assess changes in fluid volumes, CNVM volumes, fibrin, etc. We may be on the verge of this, based on the technological advances in OCT image analysis. It is likely, however, that our current biomarkers (FA and 2-dimensional OCT) are inadequate for this combined therapy.

MARCO ZARBIN: The other secondary variables we look at when assessing success are all very exciting, but not as relevant. There is a lack of precision in those variables because the judgments we make about the size, morphology, and disappearance of lesions are, to some degree, all subjective. And there is lack of tight agreement among observers on those issues.

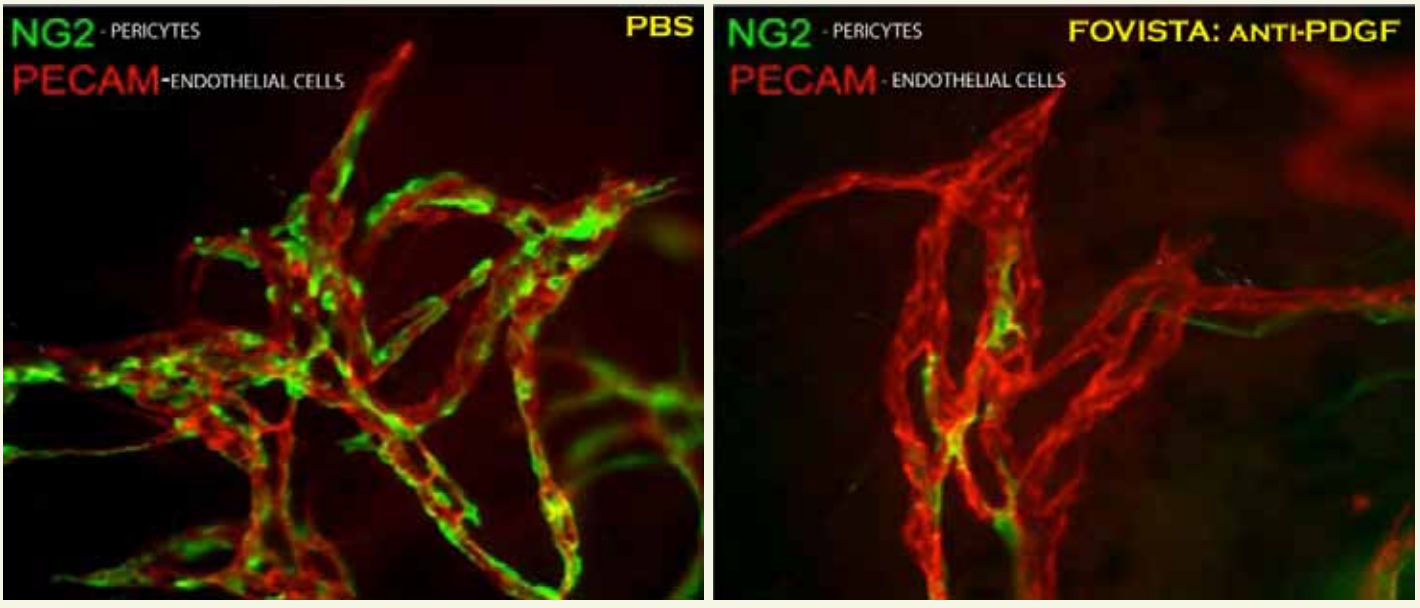

FIGURE 4 Pericyte coverage (green stain) of a neovascular complex before (left) and after (right) Fovista combination therapy.

I think FA is on the way out. Unpublished and published data I have examined lead me to believe that OCT image analysis from the mathematically reconfigured data/Doppler effect could image retinal and choroidal vessels with a degree of resolution that rivals and exceeds that of FA. This may not be ready today, but I believe it is the future. Even with the technology available today, the vast majority of treatment decisions, in my experience, are based on OCT-derived data.

'Not only is combination therapy going to make the patient see better, but it could change the logistical burden and cost of treatment.'

—Marco A. Zarbin, MD, PhD

ELIAS REICHEL: The reading center observed some intriguing findings relating to highly reflective spots seen in neovascular complexes on spectral domain OCT images. In eyes that showed the most visual improvement after being treated with Fovista and Lucentis, there was a trend for these spots to go away. This was seen more with combination treatment than with monotherapy.

Future studies may indicate that these highly reflective spots serve as a useful biomarker in following these patients and may be helpful in determining the need for retreatment. This is a profound observation. Further, the neovascular regression data in visual gainers and losers are in line with what one would expect, given the current state of FA technology.

PRAVIN DUGEL: I agree that FA is not ideal to assess the treatment regimen.

What are the key shortcomings of fluorescein angiography?

KARL CSAKY: Fluorescein is a small molecule (400 to 500 daltons) and is not protein bound. It leaks out and interacts with diseased blood vessels and tissue in a variety of staining patterns. Within these altered tissues, it is very hard for the retina specialist and/or reading center to precisely delineate small changes in the presence or measurement of blood vessels within the heterogeneous fluorescein patterns. While FA is quite *sensitive*, it is not *specific*. For reading centers, it is to some extent, like a Rorschach test—to give an impression of what one sees.

I have examined the 1-year FA data for the same agent (Lucentis 0.5 mg q 4 months administered for 12 months) in wet-AMD patients read by 2 different reading centers (for the ANCHOR and HARBOR trials). The results, interestingly, were dissimilar. Therefore, there is significant variability in FA assessment of the CNVM size, depending on the criteria reading centers use to measure the size of CNVM. In the ANCHOR and HARBOR trials, the correlation of visual outcome to CNVM regression and growth was poor—especially in patients with moderate visual improvement (< 15 letters gained). There was some suggestion of correlation of neovascular regression and visual gain at the extreme (15 or more letters gained).

A similar pattern is noted in this Fovista phase 2b trial, where greater neovascular regression in the anti-PDGF combination arm was seen than in Lucentis monotherapy arm for patients in the 15-letters or greater gain. In moderate visual gain patients, a lesser difference was noted. Presumably, the noise level is high in the moderate visual gain group. The FA pattern for anti-PDGF/combination therapy-mediated CNVM change is unknown. We do not know what the fingerprint should be for vessels that disappear but still have remnants of injury.

In indocyanine green (ICG) imaging, the larger molecular weight dye is protein bound and provides better outlines for the CNVM. However, it is not as sensitive as fluorescein. ICG may provide better and more precise information for the change in CNVM size, but this is not known. Our current biomarkers are imprecise at best for anti-VEGF monotherapy, but may be inappropriate for anti-PDGF combination therapy as well.

'Relative vision improvement of approximately 62% is impressive.'

—David S. Boyer, MD

GLENN JAFFE: FA has inherent variability. There is significant variability in assessment and quantification of leakage patterns, staining, and intensity of fluorescence. These parameters change at different time points in a given patient and vary considerably when comparing the same time points between patients.

There also is considerable variability across different reading centers. Despite this inherent variability, in this Fovista/anti-VEGF combination phase 2b trial, it is exciting that the FA results correlated with trends in the gainers and losers of visual function.

'...SHRM's thickness appears to correlate with visual function. Therefore it is reasonable to hypothesize that if a drug caused reduced SHRM, visual improvement could ensue.'

—Glenn J. Jaffe, MD

PRAVIN DUGEL: A number of consequential points deserve further emphasis:

- **The appropriate biomarkers for anti-PDGF combination therapy are not known with our current technology.**
- **FA-guided CNVM lesion size change has significant variability in measurement and as expected, cannot serve as a surrogate for visual function.**
- **Despite these variables the subgroup analyses in the Fovista trial are remarkably consistent in correlating with significant vision improvement and vision loss.**

'If [the phase 2b trial] results are confirmed in a phase 3 pivotal trial, Fovista combination therapy will change our current treatment model in patients with neovascular macular degeneration.'

— Pravin U. Dugel, MD

The subanalyses included patients:

- Gaining 3 or more lines of vision
- With 20/40 or better vision
- With 20/25 or better vision
- Losing 1 line or more of vision
- With final visual acuity of 20/200 or worse

All of these subgroup analyses correlated with vision. The remarkable and correlative OCT biomarker results of SHRM to visual function in this trial may guide our future treatment regimen.

Vision improvement is paramount and efficacy is king. Who would withhold therapy to improve vision by an additional 62%? In this phase 2b Fovista combination trial—the largest superiority phase 2b trial ever done in retina—the visual efficacy results are overwhelmingly positive and show remarkable consistency. If these results are confirmed in a phase 3 pivotal trial, Fovista combination therapy will change our current treatment model in patients with neovascular macular degeneration.

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Financial Disclosures

Dr. Dugel – ABBOTT LABORATORIES: Consultant, Honoraria; ALCON LABORATORIES, INC: Consultant, Honoraria; ALLERGAN, INC: Consultant, Honoraria; ARCTICDX: Consultant, Honoraria, Stockholder, Stock; GENENTECH: Consultant, Honoraria; MACUSIGHT, INC: Consultant, Honoraria, Stockholder, Stock; NEOVISTA, INC: Consultant, Honoraria, Stockholder, Stock; ORA: Consultant, Honoraria; THROMBOGENICS: Consultant, Honoraria; REGENERON PHARMACEUTICALS, INC: Consultant, Honoraria; OPHTHOTECH CORPORATION: Consultant, Minor Equity Position.

Dr. Reichel – HEMERA BIOSCIENCES INC: Founder, Stock; AKORN, INC: Other, Royalty; ALLERGAN, INC: Advisory Board, Investigator, Honoraria; OPHTHOTECH CORPORATION: Consultant, Stock; EMD SERONO, INC: Consultant, Honoraria; GLAXOSMITHKLINE: Consultant, Investigator, Honoraria; NEOVISTA, INC: Consultant, Honoraria, Stock; REGENERON PHARMACEUTICALS, INC: Advisory Board, Investigator, Speaker, Honoraria; GENENTECH: Consultant, Investigator, Honoraria; PERCEPTIVE INFORMATICS: Consultant, Honoraria; OCULAR INSTRUMENTS: Other, Royalty; EPSILON INSTRUMENTS: Other, Royalty; THROMBOGENICS: Advisory Board, Consultant, Investigator, Grants, Honoraria; FALCK MEDICAL, INC: Advisory Board, Investigator, Other, Grants; ALIMERA SCIENCES: Advisory Board, Investigator, Grants, Honoraria.

Dr. Duker – HEMERA BIOSCIENCES: Founder, Stock; OPHTHOTECH CORPORATION: Consultant, Stock; EYENETRA: Consultant, Stock; PALOMA PHARMACEUTICALS: Advisory Board, No Compensation Received; EMD/SERONO: Consultant, Honoraria; GENENTECH: Consultant, Honoraria; ALCON LABORATORIES, INC: Consultant, Honoraria; REGENERON PHARMACEUTICALS, INC: Consultant, Honoraria; THROMBOGENICS: Consultant, Honoraria; CARL ZEISS MEDITEC: Other, Equipment (Department or Practice); TOPCON MEDICAL SYSTEMS, INC: Other, Equipment (Department or Practice); OPTOVUE: Other, Equipment (Department or Practice); NEOVISTA, INC: Advisory Board, Honoraria; NOVARTIS PHARMACEUTICALS CORPORATION: Consultant, Honoraria; QLT INC: Consultant, Honoraria.

Dr. Boyer – ALCON LABORATORIES, INC: Advisory Board, Consultant, Investigator, Speaker, Grants, Honoraria; ALLERGAN, INC: Advisory Board, Consultant, Investigator, Speaker, Grants, Honoraria; ALLEGRO OPHTHALMICS: Advisory Board, Stockholder, Honoraria; GENENTECH: Consultant, Investigator, Speaker, Grants, Honoraria; REGENERON PHARMACEUTICALS, INC: Consultant, Investigator, Grants, Honoraria; iCo THERAPEUTICS INC: Consultant, Investigator, No Compensation Received; GLAXOSMITHKLINE: Consultant, Honoraria; NOVARTIS PHARMACEUTICALS CORPORATION: Consultant, Investigator, Grants, Honoraria; BAYER HEALTHCARE: Consultant, Honoraria; QUARK PHARMACEUTICALS, INC: Investigator, Grants.

Dr. Jaffe – ABBOTT LABORATORIES: Consultant, Honoraria; NEUROTECH INC: Consultant, Honoraria; HEIDELBERG ENGINEERING: Consultant, Honoraria; PSIVIDA: Consultant, Grants.

Dr. Zarbin – ALIMERA SCIENCES: Consultant, Honoraria; IMAGEN BIOTECH, INC: Consultant, Honoraria; IRIDEX CORPORATION: Consultant, Honoraria; NOVARTIS PHARMA AG: Consultant, Honoraria; PFIZER INC: Consultant, Honoraria.

Dr. Csaky – GENENTECH: Advisory Board, Consultant, Investigator, Speaker, Grants, Honoraria; HEIDELBERG ENGINEERING: Advisory Board, Honoraria; QLT INC: Advisory Board, Consultant, Honoraria; NOVARTIS PHARMACEUTICALS CORPORATION: Consultant, Honoraria; ACUCELA INC: Advisory Board, Consultant, Honoraria; OPHTHOTECH CORPORATION: Consultant, Honoraria, Stock Options; SANTEN PHARMACEUTICALS: Consultant, Honoraria.