touchCONGRESS from the World Ophthalmology Congress 2020 (WOC2020 Virtual®)

The personalized patient experience in nAMD

Prof. Pravin Dugel
Clinical Professor, USC Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

Webinar recorded July 2020

nAMD, neovascular age-related macular degeneration

Funded by an independent medical education request from Novartis

Disclaimer

Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions.

The presenting faculty have been advised by touchIME to ensure that they disclose any such references made to unlabelled or unapproved use.

No endorsement by touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in touchIME activities.

touchIME accepts no responsibility for errors or omissions.

Webinar overview

The personalized patient experience in nAMD

- Introduction
- Part 1: WOC2020 Virtual® congress symposia highlights
- Part 2: WOC2020 Virtual® congress abstracts

nAMD, neovascular age-related macular degeneration; WOC2020, World Ophthalmology Congress 2020.

Introduction

The personalized patient experience in nAMD

- A heterogeneous patient population with wide variations according to treatment intensity needed
- Duration of VEGF suppression varies among patients
- Any fluid accumulation indicates disease activity that requires more intensive anti-VEGF therapy
- Close monitoring with zero-tolerance for fluid has become the principle of OCT monitoring
- Matching an individual patient to the appropriate anti-VEGF agent, dosing approach and dosing interval is critical
- State-of-the-art management approaches are needed to reduce treatment burden for individual patients
- Today we will discuss recent data presented at the WOC2020 and how they may impact what we are currently doing in the clinic

nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; VEGF, vascular endothelial growth factor; WOC2020, World Ophthalmology Congress 2020.

Holekamp NM. *Am J Manag Care*. 2019;25:S172–81.

WOC2020 Virtual® congress symposia highlights

Focus on novel and emerging therapies and retinal fluid management

nAMD, neovascular age-related macular degeneration; WOC2020, World Ophthalmology Congress 2020.

touch OPHTHALMOLOGY®

Novel and emerging therapies

Novel and emerging therapies for the treatment of nAMD were discussed in the following sessions at WOC2020 Virtual:

- Symposium: Innovation in retina
  - Emerging therapies for wet AMD by Andrew Moshfeghi
- Symposium: Latest developments in medical retina
  - Novel long-duration drugs in retinal disease by Francesco Bandello
- Symposium: Management of age-related macular degeneration
  - Gene therapy for AMD by Allen Ho
  - Brolucizumab in the current management of nAMD by SriniVas Sadda
- Symposium: The new global retina revolution: 2020 and beyond
  - Next generation anti-VEGF therapies by Peter Kaiser

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor; WOC, World Ophthalmology Congress.

Novel and emerging therapies for nAMD: Overview

Anti-VEGF	Bispecific antibodies	Antibody biopolymer conjugate	Gene therapy
• Brolucizumab • Abicipar pegol • Conbercept	• Faricimab	• KS-301	• RGX314 • ADVM-022

- The structure, binding properties and MOA of novel anti-VEGF therapies in clinical development were reviewed in detail by Peter Kaiser in his presentation “Next generation anti-VEGF therapies”
- Most of the discussion at WOC2020 Virtual focussed on recent clinical experience with brolucizumab and the latest updates on abicipar pegol

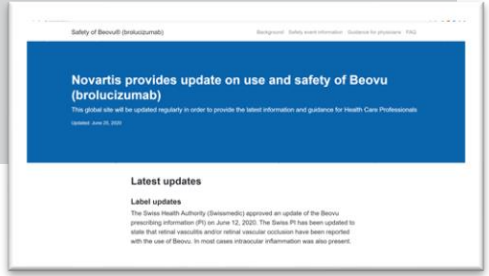
MOA, mechanism of action; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor; WOC2020, World Ophthalmology Congress 2020.

Novel and emerging therapies: Brolucizumab

Presentations on brolucizumab focussed on reviewing long-term safety and efficacy data from the HAWK and HARRIER phase III trials

- Secondary outcomes highlighting the greater reductions in retinal fluid observed with brolucizumab compared with aflibercept were considered particularly interesting given the importance of removing retinal fluid to long-term outcomes in patients with nAMD
- Updates on the risk of intraocular inflammation were provided following post-marketing reports of severe inflammation and/or occlusive retinal vasculitis

Further information can be found at www.brolucizumab.info



Resolving retinal fluid is key to reducing burden of nAMD treatment

In both HAWK and HARRIER, compared with aflibercept, patients on brolucizumab had significantly less:

- Disease activity at Week 16 for the 6 mg dose, as assessed by masked investigator
- IRF and/or SRF fluid at Weeks 16, 48 and 96
- Sub-RPE fluid at Weeks 16, 48 and 96

In an FDA label update (Oct 2019) based on HAWK and HARRIER the risk of intraocular inflammation was 4%, with a 1% risk of retinal artery occlusion

"Broculizumab in the current management of nAMD" by SriniVas Sadda. WOC2020 Virtual, 26–29 June 2020.
FDA, US Food and Drug Administration; IRF, intraretinal fluid; nAMD, neovascular age-related macular degeneration; RPE, retinal pigment epithelium; SRF, subretinal fluid.

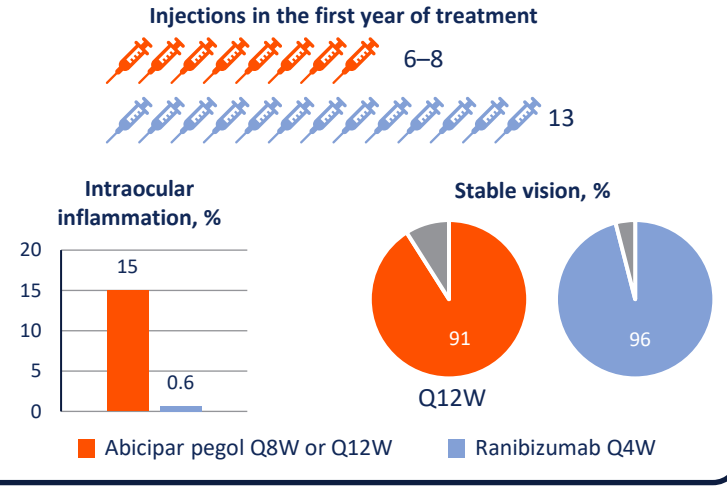
Novel and emerging therapies: Abicipar pegol

WOC2020 Virtual coincided with release of a Complete Response Letter for abicipar pegol by the FDA[1]

"Emerging therapies for wet AMD" by Dr Andrew Moshfeghi

- Despite promising results demonstrating similar efficacy to ranibizumab with a reduced number of injections, the FDA indicated that the rate of intraocular inflammation observed following administration of abicipar pegol 2 mg/0.05 ml results in an unfavourable benefit–risk ratio
- Discussions at WOC2020 Virtual suggested that manufacturing improvements may reduce incidence of ocular inflammation with abicipar pegol

SEQUOIA & CEDAR phase III studies of apicipar pegol for the treatment of nAMD



"Emerging therapies for wet AMD" by Dr Andrew Moshfeghi WOC2020 Virtual, 26–29 June 2020.
FDA, US Food and Drug Administration; nAMD, neovascular age-related macular degeneration; Q4/8/12W, every 4/8/12 weeks; WOC2020, World Ophthalmology Congress 2020.
1. Press release. Abbvie 26 June 2020. Allergan, an AbbVie Company, and Molecular Partners receive complete response letter from FDA on biologics license application for abicipar pegol. Available at: https://news.abbvie.com/news/press-releases/allergan-an-abbvie-company-and-molecular-partners-receive-complete-response-letter-from-fda-on-biologics-license-application-for-abicipar-pegol.htm (accessed 30 July 2020).

Novel and emerging therapies for nAMD: Other agents

Anti-VEGF	Bispecific antibodies	Antibody biopolymer conjugate	Gene therapy
• Brolucizumab • Abicipar pegol • Conbercept	• Faricimab	• KS-301	• RGX314 • ADVM-022

- Allen Ho provided an update on the latest data and developments with gene therapy for the treatment of nAMD, focussing on RGX314
  - RGX314 was well tolerated at all dose levels with a long-term, durable treatment effect over 2 years
  - Subretinal administration is the established route; suprachoroidal space administration has the potential to be the preferred choice for in-office administration
- Data from the phase II STAIRWAY trial of faricimab were briefly highlighted by Andrew Moshfeghi in his presentation titled “Emerging therapies for nAMD”

nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

Management of retinal fluid in nAMD

The management of retinal fluid in nAMD was discussed in the following sessions at WOC2020 Virtual:

- Symposium: The new global retina revolution: 2020 and beyond
  - Residual fluid and anatomic correlates in the treatment of nAMD by SriniVas Sadda
- Symposium: Retinal pharmacology: Where are we going now?
  - Fluid management in nAMD by SriniVas Sadda

nAMD, neovascular age-related macular degeneration; WOC, World Ophthalmology Congress.

Management of retinal fluid in nAMD

Review of evidence informing the management of retinal fluid in nAMD from MARINA and ANCHOR to the present day

“Fluid management in neovascular AMD” by Dr SriniVas Sadda

- Since the advent of anti-VEGF therapy the standard approach has been to control exudation and dry the retina using anti-VEGF therapy
- Residual fluid has been associated with reduced vision and more recently data from HAWK and HARRIER has confirmed an association between fluctuating CRT and vision loss
- On the contrary, data from HARBOR and other trials have suggested that residual sub-retinal fluid may be protective against development of atrophy
  - Association does not equal causation: patients were being treated with the aim of drying the retina
  - Current hypothesis is that residual sub-retinal fluid may be a sign of CNV membrane survival and a persistent but controlled type 1 CNV with intact RPE may protect the retina from atrophy

Recommendations for clinical practice

- With the advent of anti-VEGF therapy, vision gain following treatment is the new standard
  - Undertreatment of nAMD consistently results in sub-optimal outcomes
- The best evidence supports maintaining a dry retina
  - Treat without extending when residual fluid is present
  - Sub-retinal residual fluid does not prevent patients achieving good visual outcomes
  - Intra-retinal fluid is usually associated with poorer long-term visual outcomes
- Alternate diagnoses should be considered in cases of persistent residual fluid that does not respond to anti-VEGF therapy

“Fluid management in neovascular AMD” by Dr SriniVas Sadda. WOC2020 Virtual, 26–29 June 2020.
nAMD, neovascular age-related macular degeneration; CNV, choroidal neovascularisation; CRT, central retinal thickness; RPE, retinal pigment epithelium; VEGF, vascular endothelial growth factor.

WOC2020 Virtual® congress symposia highlights

Focus on drug delivery devices and home monitoring

nAMD, neovascular age-related macular degeneration; WOC2020, World Ophthalmology Congress 2020.

touch OPHTHALMOLOGY®

Ocular drug delivery systems including port delivery

Ocular drug delivery systems and their place in the treatment of nAMD were discussed in the following sessions at WOC2020 Virtual:

- Symposium: Latest developments in medical retina
  - Slow-release devices in AMD by Dante J Pieramici
- Symposium: The new global retina revolution: 2020 and beyond
  - Towards more durable anti-VEGF therapy for neovascular AMD: port delivery by Dante J Pieramici
  - Updates on ocular drug delivery systems by Jennifer Kang-Mieler

nAMD, neovascular age-related macular degeneration; VEGF,vascular endothelial growth factor; WOC2020, World Ophthalmology Congress 2020.

Ocular drug delivery systems including port delivery

Update on the port delivery system with ranibizumab

"Towards more durable anti-VEGF therapy for neovascular AMD: port delivery" by Dr Dante Pieramici

- Details and videos of the surgical procedures required to insert the PDS were shared, including the amendments made to reduce incidence of vitreous haemorrhage
- The office-based refill procedure was reviewed
- Dr Pieramici commented that in his experience, as part of the ARCHWAY phase III trial of the PDS, although the refill procedure is more challenging than intravitreal injections for physicians, patients find the process much easier and more convenient

The PDS with Ranibizumab

The PDS is a drug delivery reservoir currently in phase III trials

- Refillable intraocular implant
- Permanently situated at the pars plana
- Surgical insertion
- Refills can be performed in office
- Ranibizumab (customized formulation) continuously delivered into the vitreous humour

"Towards more durable anti-VEGF therapy for neovascular AMD: port delivery" by Dr Dante Pieramici. WOC2020 Virtual, 26–29 June 2020.
AMD, age-related macular degeneration; PDS, port delivery system with ranibizumab.
Press release: Genentech 26th May 2020. Port Delivery System With Ranibizumab Shows Positive Phase III Results in Neovascular Age-Related Macular Degeneration. Available at: https://www.gene.com/media/press-releases/14854/2020-05-26/port-delivery-system-with-ranibizumab-sh

Ocular drug delivery systems including port delivery

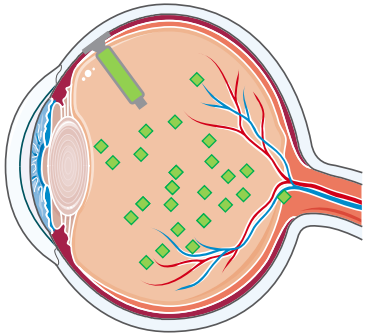
Update on the port delivery system with ranibizumab

- A detailed analysis of the PK profile of the PDS from the LADDER trial highlighted that the serum PK profile of ranibizumab reflects the implant release rate:

Implant release rate
<
Ocular elimination rate
<
Systemic elimination rate

- Serum ranibizumab concentrations achieved with PDS 100 mg/ml were within the range seen with monthly intravitreal ranibizumab 0.5 mg

Continuous delivery of ranibizumab from the PDS is mediated by passive diffusion



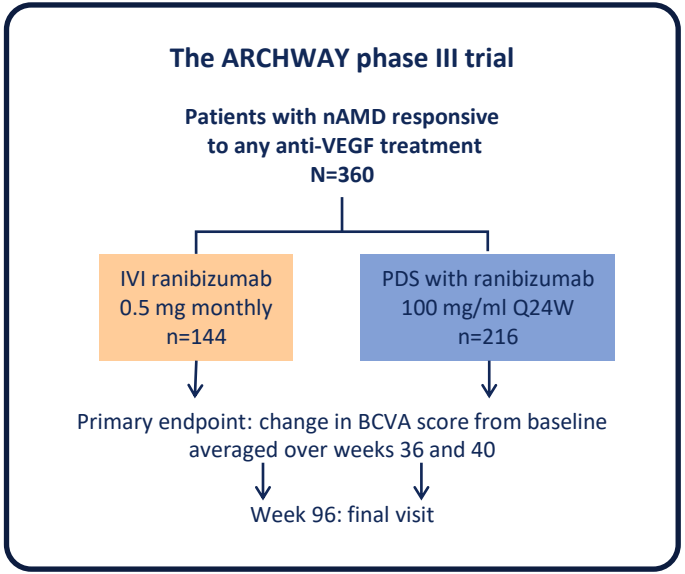
"Towards more durable anti-VEGF therapy for neovascular AMD: port delivery" by Dr Dante Pieramici. WOC2020 Virtual, 26–29 June 2020.
PDS, port delivery system with ranibizumab; PK, pharmacokinetics.

Ocular drug delivery systems including port delivery

Update on the port delivery system with ranibizumab

Dr Dante Pieramici commented:

- The ARCHWAY phase III trial results, which will be released shortly, look very positive with the trial meeting its primary endpoint, demonstrating that patients with PDS who received refills every 6 months achieved visual acuity outcomes equivalent to those receiving monthly ranibizumab 0.5 mg injections[1]
- PDS is unlikely to be used in newly diagnosed patients, but could particularly suit patients who need anti-VEGF treatment every 4–6 weeks
- PDS could provide an additional option to enable physicians to tailor therapies to patients' individual needs, reducing the burden of frequent injections in patients who are high users of VEGF therapy



BCVA, best corrected visual acuity; IVI, intravitreal injection; nAMD, neovascular age-related macular degeneration; PDS, port delivery system with ranibizumab; PK, pharmacokinetics; VEGF, vascular endothelial growth factor. Press release: Genentech 26th May 2020. Port Delivery System With Ranibizumab Shows Positive Phase III Results in Neovascular Age-Related Macular Degeneration. Available at: https://www.gene.com/media/press-releases/14854/2020-05-26/port-delivery-system-with-ranibizumab-sh (accessed 30 June 2020).

Ocular drug delivery systems including port delivery

Review of microsphere-hydrogel delivery system in development for the treatment of nAMD with anti-VEGF therapy

"Updates on ocular drug delivery systems" by Dr Jennifer J. Kang-Mieler

- The microsphere-hydrogel DDS combines biodegradable microspheres of encapsulated aflibercept with a thermo-responsive hydrogel
  - The hydrogel confines the microspheres to a specific delivery site
  - Data from rodent and non-human primate models suggest potential for sustained drug delivery with no indication of ocular safety concerns[1,2]

The microsphere-hydrogel DDS

- In vitro aflibercept was released from the degradable microsphere-hydrogel DDS and remained bioactive for over 200 days[3]
- In a rodent model of CNV lesions a single injection of aflibercept-loaded microsphere hydrogel DDS equivalent to 1 µg aflibercept resulted in reductions in CNV lesion area that were sustained through 22 weeks
- There were no changes in intraocular pressure, retinal function (ERG) or retinal thickness (OCT) or markers of inflammatory response in trials of the microsphere hydrogel DDS in a non-human primate model

"Updates on ocular drug delivery systems" by Dr Jennifer J. Kang-Mieler. WOC2020 Virtual, 26–29 June 2020.
CNV, choroidal neovascularization; DDS, drug delivery system; ERG, electroretinogram; nAMD, neovascular age-related macular degeneration; PDS, port delivery system with ranibizumab; OCT, optical coherence tomography; VEGF, vascular endothelia growth factor.
1. Osswald CR and Kang-Mieler J. *Curr Eye Res.* 2016;41:1216–22; 2. Osswald CR et al. *Curr Eye Res.* 2017;42:1293–301; 3. Liu W, et al. *Curr Eye Res.* 2019;44:264–74.

Home monitoring of nAMD

The potential place of home monitoring in the management of nAMD was discussed in the following sessions at WOC2020 Virtual®:

- Symposium: Current evidence for managing retinal disease
  - We are ready for home monitoring of nAMD patients on follow up? Debate between Dawn Sim and Francesco Bandello
- Symposium: Latest developments in medical retina
  - Monitoring by home OCT in AMD by Anat Loewenstein

nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; WOC, World Ophthalmology Congress.

Home monitoring of nAMD

We are ready for home monitoring of NVAMD patients on follow up

Yes: Dawn Sim

- The AREDS2-HOME study demonstrated a smaller loss in visual acuity between baseline and CNV detection in patients using a home monitoring strategy (-4 letters) compared with standard of care (-9 letters)[1]
- Increased use of smartphones and similar devices may enable us to use technology to monitor patients with nAMD at home
- Apps allow thresholding, monitoring and instant feedback to patients and scores can be monitored by physicians
- A smartphone and web-based app has been successfully used to monitor patients with nAMD during COVID-19 lockdown by Moorfields Eye Hospital, London, UK
- With reduced clinic capacity for the foreseeable future we must find ways to monitor patients at home

No: Francesco Bandello

- Early detection of disease activity and consequent anti-VEGF therapy is critical to maintaining visual function
- Patient-related limitations and technical difficulties limit uptake of home monitoring technologies in the real world
- Home monitoring can be a beneficial addition to clinical evaluation but we are not ready for home monitoring only

"We are ready for home monitoring of NVAMD patients on follow up" by Dawn Sim and Francesco Bandello. WOC2020 Virtual, 26–29 June 2020.
CNV, choroidal neovascularisation; nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor.

1. AREDS2-HOME study research group, et al. *Ophthalmology.* 2014; 121:535–44.

Home OCT monitoring of nAMD

Update on the potential of home OCT monitoring to catch disease recurrence or progression as soon as it happens

“Monitoring by home OCT in AMD” by Dr Anat Lowenstein

- By providing patients and physicians with unique inter-visit disease knowledge, home OCT monitoring offers improved personalization of treatment regimens
  - Under the PRN approach, using daily at-home test, patients can be treated as soon as fluid is detected, reducing the number of days with fluid present, limiting under treatment and improving visual acuity outcomes
  - Home monitoring may also benefit a T&E approach, supporting accelerated extension to reduce treatment burden
- As longer-acting anti-VEGF treatments become available, home OCT monitoring may assist with determining personalized re-dosing frequency and could act as a safety net between extended in-office visits

A comparison of the Notal Home OCT device with a commercial in-office OCT system was presented

- Patients aged 45–99 years, some with low visual acuity
- High sensitivity (91%) and specificity (97%) for the detection of retinal fluid
- High level of patient satisfaction
- 90% of patients successfully self-operated the device
- Similar quality of image to commercial in-office OCT
- Supported by:
  - Validated algorithm to provide AI-based automated data analysis
  - Infrastructure to directly interact with patients

“Monitoring by home OCT in AMD” by Dr Anat Lowenstein. WOC2020 Virtual, 26–29 June 2020.
AI, artificial intelligence; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; PRN, pro re nata; T&E, treat and extend; VEGF, vascular endothelial growth factor.

Summary

- Data presented at WOC2020 Virtual demonstrate that the recent approvals and emerging techniques and therapies hold the potential to allow true personalization of care for patients with nAMD
- Although intraocular inflammation is a concern, both brolucizumab and abicipar pegol have demonstrated their potential to maintain visual function with fewer injections, reducing the burden of therapy on patients, physicians and the healthcare system
- In addition to long-acting therapies, WOC2020 Virtual provided updates on novel technologies, such as the PDS with ranubizumab, that have the potential to significantly reduce the burden of therapy, particularly in patients who need frequent anti-VEGF therapy injections
- Increased use of home monitoring systems has the potential to synergize with all treatment schedules and types of therapy to facilitate prompt identification of disease activity, support T&E protocols and improve outcomes for patients

nAMD, neovascular age-related macular degeneration; PDS, port delivery system; T&E, treat-and-extend; VEGF, vascular endothelial growth factor; WOC, World Ophthalmology Congress.

WOC2020 Virtual® congress abstracts

Focus on treatments for nAMD

nAMD, neovascular age-related macular degeneration

touch OPHTHALMOLOGY®

Disease activity assessments with brolucizumab vs aflibercept in patients with nAMD in HAWK and HARRIER

Hamilton R, et al.

To compare the presence of disease activity in patients with nAMD treated with brolucizumab or aflibercept in the HAWK and HARRIER phase III trials

Methodology

- Patients were randomized equally between treatment groups (n=1,088 HAWK; n=729 HARRIER)
- After 3 monthly loading doses patients received Bro Q12W unless DA was detected at any predefined DAA; presence of DA resulted in permanent Q8W dosing
- Dosing of Afl was fixed at Q8W

	HAWK			HARRIER	
	Bro 3 mg	Bro 6 mg	Afl 2 mg	Bro 6 mg	Afl 2 mg
DA at W16, % patients	28.1*	24.0**	34.5	22.7**	32.2
DAA at which DA detected, %	14.9	13.6	22.2	15.7	19.6

	HAWK	HARRIER
Probability of a 6 mg patient maintaining a Q12W interval after loading to:		
W48, % patients	56	51
W96, % patients	45	39
If the first Q12W interval was successfully completed, probability of remaining on a Q12W interval to W48, % patients	85	82
If W48 was successfully completed on a Q12W interval, probability of remaining on a Q12W interval to W96, % patients	>80	>75

Overall, the safety profile of brolucizumab was well tolerated. In a post-marketing update a safety signal of rare adverse events of retinal vasculitis and/or RVO, which may result in severe vision loss was identified

In the HAWK and HARRIER clinical trials, patients treated with brolucizumab had a lower risk of disease activity occurrence and therefore better disease control compared with aflibercept

Afl, aflibercept; Bro, brolucizumab; DA, disease activity; DAA, disease activity assessment; nAMD, neovascular age-related macular degeneration; Q8W, every 8 weeks; Q12W, every 12 weeks; RVO, retinal vein occlusion; W, week. *p<0.0013, **p<0.0021 vs aflibercept

Hamilton R, et al. Abstract presented at WOC2020 Virtual, 26–29 June 2020. [Abstract OP-094].

touch OPHTHALMOLOGY®

Association of CST variability and VFQ-25 scores in nAMD: 96-week pooled analyses from the HAWK and HARRIER trials

Dugel P, et al.

To explore the association between NEI VFQ-25 outcomes and CST in a post-hoc analysis of pooled brolucizumab and aflibercept data from the HAWK and HARRIER trials in patients with AMD

Methodology

- Treatment agnostic approach
- CST SD was categorised into four quartiles of increasing variability, with approx. 400 patients in each quartile
- Relationship between CST variability and NEI VFQ-25, and four specific subscales of NEI VFQ-25 over 96 weeks of study treatment was explored
- NEI VFQ-25 subscales
  - Dependency
  - Role difficulties
  - Distance activities
  - Near activities

Results

- Patients with less CST variability had:
  - A higher improvement in mean NEI VFQ-25 scores from baseline to W96
  - Better scores across the four specific NEI VFQ-25 subscales from baseline to W96
- Across mean total and subscales scores, the relationship between lower CST variability and higher NEI VFQ-25 was apparent in post-loading dose data from Weeks 12–96 excluding and impact of initial fluctuation during the loading phase

Overall, the safety profile of brolucizumab was well tolerated. In a post-marketing update a safety signal of rare adverse events of retinal vasculitis and/or RVO which may result in severe vision loss was identified

Provides a unique insight into the association between anatomical outcomes and patient-reported outcomes. Better NEI VFQ-25 scores, and specifically outcomes on subscales reflective on important activities of daily life, were associated with better controlled CST

CST, central subfield thickness; nAMD, neovascular age-related macular degeneration; NEI, National Eye Institute; RVO, retinal vein occlusion; SD, standard deviation; VFQ, vision function questionnaire; W, week.

Dugel P, et al. Abstract presented at WOC2020 Virtual, 26–29 June 2020. [Abstract OP-092].

touch OPHTHALMOLOGY®

Treat-and-extend intravitreal aflibercept for nAMD: 2-year ARIES study results

Wolf S, et al.

To assess whether aflibercept administered in an early T&E regimen was non-inferior to a late-start T&E regimen in patients with nAMD after 104 weeks of treatment

Methodology

- All patients received three initial monthly doses of 2 mg Afl plus an injection at W16
- At W16 patients were randomized 1:1 to
  - Early start T&E: T&E regimen extended by 2 weeks or an initial 4 week interval to a maximum of 16 weeks
  - Late start T&E: Afl Q8W to W52 followed by T&E regimen
- Primary endpoint: Mean change in BCVA (EDTRS letters) from W16 to W104

	Early T&E	Late T&E
BCVA		
ETDRS letters, mean change from baseline, letters	-2.1*	-0.4
<15 ETDRS letter loss, % patients	93.4	96.2
≥15 EDTRS letter gain, % patients	18.9	22.1
CRT, mean change from baseline, µm	-161.5	-158.6
No. of injections, mean	12	13
Last injection interval ≥12 weeks, % patients	47.2	51.9

- BCVA change between the two treatment regimens was statistically non-inferior
- Most patients maintained vision
- No strong predictors for long injection-interval patterns were identified: CST at W16 showed the highest association
- Safety profile was consistent with results from prior studies of Afl

Functional and anatomical outcomes were consistent between early- and late-start T&E aflibercept regimens for the treatment of nAMD. The mean reduction in the number of injections with early start T&E was clinically relevant.

Afl, aflibercept; BCVA, best corrected visual acuity; CST, central subfield thickness; CRT, central retinal thickness; EDTRS, Early Treatment Diabetic Retinopathy Study; nAMD, neovascular age-related macular degeneration; Q8W, every 8 weeks; T&E, treat and extend; W, week. *p<0.05 for non-inferiority

Wolf S, et al. Abstract presented at WOC2020 Virtual, 26–29 June 2020. [Abstract OP-095].

Conbercept in the management of nAMD and PCV

Heier and Kaiser.

To describe the clinical development of conbercept, a recombinant VEGFR fusion protein first approved for the treatment of nAMD in China in 2013

Conbercept binds to all isoforms of VEGF-A as well as VEGF-B, VEGF-C and PIGF with picomolar affinity preventing binding of VEGF to both VEGFR-1 and VEGFR-2

The structure of conbercept is similar to aflibercept, with the addition of a fourth domain which results in:

- **Increased binding capacity for VEGF**
- **Prolonged clearance time**

PHOENIX

Phase III clinical trial in 124 Chinese patients with AMD across 9 centres in China

- 0.5 mg conbercept Q4W x 3 then Q12W
- Primary endpoint was mean improvement in BCVA (letters) at month 3
  - 9.1 letters conbercept 0.5 mg vs 2.0 letters sham injection
- After 12 months treatment mean change in BCVA (letters) was 9.9 in patients receiving conbercept throughout
- The incidence of AEs was low with no cardiovascular or cerebrovascular AEs

PANDA

Worldwide multi-centre, non-inferiority phase III trial to evaluate the efficacy and safety of conbercept compared with aflibercept in patients with nAMD

- Patients randomized in a 1:1:1 ratio to
  - 0.5 mg conbercept Q4W loading dose x 3 then Q8W
  - 1.0 mg conbercept Q4W loading dose x 3 then Q12W
  - 2.0 mg aflibercept Q4W loading dose x 3 then Q8W
- Primary outcome: Mean change from baseline in BCVA at week 36 in the study eye
- Study duration is 96 weeks

Conbercept has demonstrated efficacy and safety profiles comparable to current anti-VEGF therapies and has the potential for increased durability and Q12W dosing. A worldwide phase III noninferiority study comparing conbercept with aflibercept in patients with subfoveal CNV due to nAMD is ongoing

AE, adverse event; BCVA, best corrected visual acuity; CNV, choroidal neovascularization; nAMD, neovascular age-related macular degeneration; PCV, polypoidal choroidal vasculopathy; PIGF, placental growth factor; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; VEGF, vascular endothelial growth factor; VEGF-R, vascular endothelial growth factor receptor. Heier J and Kaiser P. Abstract presented at WOC2020 Virtual, 26–29 June 2020. [Abstract OP-089].

touch OPHTHALMOLOGY®

Ladder phase II trial of the port delivery system with ranibizumab: End of study results

Dhoot DS, et al.

To compare the PDS with three different customized ranibizumab formulations with monthly intravitreal ranibizumab in patients with nAMD

Treatment, ranibizumab dose, mg/ml	PDS 10	PDS 40	PDS 100	IVI 0.5 mg
n	58	62	59	41
Age, mean years	74.4	75.0	73.5	71.9
Baseline BCVA, mean ETDRS letters score	69.3	69.9	70.4	70.6

Safety summary

- PDS was generally well tolerated with no new safety signals
- Ocular AEs of special interest were consistent with primary analysis
- Rates of cataract and systemic safety profile were similar to monthly IVI ranibizumab 0.5 mg

Treatment, ranibizumab dose, mg/ml	PDS 10	PDS 40	PDS 100	IVI 0.5 mg
Median time to first meeting refill criteria, months	8.7	13.0	15.8	n/a
Lost <5 ETDRS letters from baseline, % patients	57.7	80.0	87.5	88.9
CFT, mean change from baseline, µm	-0.7	-20.9	-4.0	-10.9
Patients not meeting refill criteria, %				
Month 6	61.6	69.6	79.8	n/a
Month 9	42.4	61.1	68.7	
Month 12	28.9	56.0	59.4	

PDS 100 mg/ml

- 79.8% patients went ≥6 months without meeting refill criteria
- BCVA and CFT results were comparable with monthly IVI ranibizumab 0.5 mg over a mean 22 months on study
- Time to first and second refill was consistent

PDS 100 mg/mL treatment maintained vision and anatomic outcomes and the optimized implant insertion procedure and refill procedure were generally well tolerated. PDS with ranibizumab has the potential to reduce high intravitreal treatment burden and improve real-world clinical outcomes

AE, adverse event; BCVA, best corrected visual acuity; CFT, central foveal thickness; ETDRS, early treatment diabetic retinopathy study; IVI, intravitreal injection; nAMD, neovascular age-related macular degeneration; PDS, port delivery system.

Dhoot DS, et al. Abstract presented at WOC2020 Virtual, 26–29 June 2020. [Abstract OP-088].

touch OPHTHALMOLOGY®

Extended Q16W dosing potential for faricimab in nAMD: STAIRWAY phase II trial

Khoramnia R, et al.

To assess dosing of faricimab, a bispecific antibody against Ang-2 and VEGF-A, at Q16W and Q12W intervals in patients with nAMD

Study design

Patients:

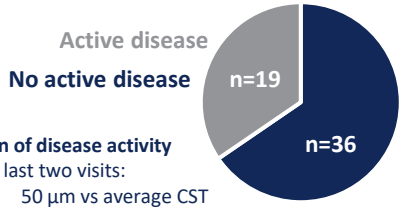
- ≥50 years
- Treatment-naïve nAMD
- Subfoveal CNV, juxtafoveal CNV with subfoveal component
- BCVA 20/40–20/320

Primary objective: efficacy of faricimab (BCVA)

Dosing:

- Faricimab 6.0 mg Q4W x 4 then Q12W
- Faricimab 6.0 mg Q4W x 4 then Q16W flex, patients with active disease at W24 switched to Q12W dosing
- Ranibizumab 0.5 mg Q4W

65% patients treated with faricimab loading doses (Q4W x 4) had no disease activity at Week 24 and could achieve Q16W dosing



Definition of disease activity

- Over last two visits:
  - ↑ 50 µm vs average CST
  - ↑ ≥75 µm over lowest CST
  - ↓ ≥5 letters of BCVA vs average
  - ↓ ≥10 letters of BCVA vs highest BCVA
- Presence of new macular haemorrhage
- Investigator opinion of significant nAMD activity that requires immediate treatment

Outcomes at W52	F Q12W	F Q16W flex	R Q4W
BCVA, mean change from baseline ETDRS letters	+10.08	+11.42	+9.59
Gain of ≥15 letters in BCVA, % patients	33.3	46.4	37.5
CST, mean change from baseline, µm	-138.5	-122.5	-129.9

Vision gains and CST reductions with Q16W flex and Q12W faricimab were comparable to Q4W ranibizumab and were maintained through W52

BVCA gains and anatomic improvements with faricimab Q16W flex and Q12W were comparable with ranibizumab Q4W treatment, with no new or unexpected safety signals. Combined inhibition of Ang-2 and VEGF-A with faricimab may extend durability of response; a global phase III clinical trial programme is ongoing

Ang-2, angiotensin-2; BCVA, best corrected visual acuity; CNV, choroidal neovascularisation; CST, central subfield thickness; ETDRS, early treatment diabetic retinopathy study; F, faricimab; nAMD, neovascular age-related macular degeneration; Q4W, every 4 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; R, ranibizumab; VEGF, vascular endothelial growth factor; W, week. Khoramnia R, et al. Abstract presented at WOC2020 Virtual, 26–29 June 2020. [Abstract OP-090].

touch OPHTHALMOLOGY®

Summary

- Abstracts presented at WOC2020 Virtual demonstrate the potential of novel therapies to expand the treatment options available to patients with nAMD
- Expanded treatment choices could reduce the burden of regular injections for patients, physicians and the healthcare system
  - Analyses from HAWK and HARRIER show that a significant number of patients could benefit from Q12W dosing of broculizumab
  - Early start T&E with aflibercept maintained visual function while reducing the mean number of injections received by patients
- Treatments and delivery systems still in development may offer future benefits
  - Phase III studies are ongoing to investigate the potential of conbercept to offer extended durability supported by Q12W dosing
  - End of study results from the LADDER trial of the Port Delivery System with ranibizumab are encouraging, with around 80% of patients going ≥6 months before meeting refill criteria. The results of the ARCHWAY study are anticipated
  - Phase II results for faricimab suggest some patients may achieve Q16W dosing and phase III trials are ongoing

nAMD, neovascular age-related macular degeneration; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend; WOC, World Ophthalmology Congress.

Thank you for watching this on-demand event

educationzone.touchophthalmology.com

touch OPHTHALMOLOGY®