Two-year results from a global observational study investigating proactive dosing regimens with intravitreal aflibercept in neovascular age-related macular degeneration (nAMD) in routine clinical practice: The XTEND study

Clare Bailey,[1] Varun Chaudhary,[2] Paul Mitchell,[3] Se Woong Kang,[4] Ramin Tadayoni,[5] Helmut Allmeier,[6] JinKyung Lee,[7] Tobias Machewitz,[7] Xin Zhang,[6] Jean-François Korobelnik,[8] on behalf of the XTEND study investigators

[1]Bristol Eye Hospital, Bristol, UK; [2]Hamilton Regional Eye Institute, St. Joseph's Healthcare Hamilton, McMaster University, Hamilton, ON, Canada; [3]University of Sydney (The Westmead Institute for Medical Research), Sydney, NSW, Australia; [4]Samsung Medical Center, Sungkyunkwan University, Seoul, Korea; [5]Université Paris Cité, AP-HP, Lariboisière, Saint Louis and Fondation, Adolphe de Rothschild Hospital, Paris, France; [6]Bayer Consumer Care AG, Basel, Switzerland; [7]Bayer AG, Berlin, Germany; [8]CHU Bordeaux, Service d'Ophtalmologie, France; Univ. Bordeaux, INSERM, Bordeaux and Population Health Research Center, team LEHA, UMR 1219, F-33000 Bordeaux, France

Presented at the Association for Research in Vision and Ophthalmology (ARVO) New Orleans, La., USA, April 23–27, 2023

Disclosures

Disclosures: Presenting author

Clare Bailey: Honoraria/attendance at advisory boards for Alimera Sciences, Apellis, Bayer, Boehringer-Ingelheim, Janssen, Novartis, and Roche

Disclosures: Co-author group

VC: Grants from Allergan Inc, Bayer Healthcare, Novartis Pharma AG, and Roche; served as a scientific advisor for Alcon Laboratories, Bayer Healthcare, Novartis Pharma AG, and Roche; **PM:** Steering Committee member for Bayer and has received consulting fees from Allergan, Bayer, and Novartis; **SWK:** Personal fees and nonfinancial support from Bayer Korea; **RT:** Board member for Alcon, Alimera, Allergan, Bausch & Lomb, Bayer, FCI, and Novartis; and a consultant for Alcon, Allergan, Bausch & Lomb, Novartis, Roche, Genentech, and Zeiss; **HA and XZ:** Employees of Bayer Consumer Care AG, Basel, Switzerland; **TM and JKL:** Employees of Bayer AG, Berlin, Germany; **J-FK:** Consultant for Allergan-AbbVie, Apellis, Bayer, Janssen, NanoRetina, Roche, Thea, and Carl Zeiss Meditec; Data and Safety Monitoring Board (DSMB) member for Alexion, and Novo Nordisk

Introduction

T&E is a proactive, individualized treatment regimen aiming to minimize the risk of disease recurrence, whilst maintaining visual gains and reducing treatment burden associated with anti-VEGF therapy

XTEND[a] is an ongoing, 36-month, multicenter, observational, prospective study recruiting patients from 127 sites in 17 countries

The **XTEND study** is examining treatment outcomes of **real-world proactive intravitreal aflibercept (IVT-AFL) treatment regimens** (fixed dosing or T&E) in treatment-naïve patients with nAMD in routine clinical practice

This analysis presents the **2-year results of the XTEND study**

[a]Evaluation of an e**X**tended and proac**T**ive dosing regim**E**n in treatment-**N**aïve patients with neovascular age-related macular **D**egeneration (nAMD). This study was initiated in May 2019 and data collection will conclude in May 2023.

nAMD, neovascular age-related macular degeneration; **T&E,** treat-and-extend; **VEGF,** vascular endothelial growth factor.

XTEND (NCT03939767) observational, prospective study design

Primary endpoint: Mean change in BCVA (ETDRS letters) from baseline to Month 12

Secondary endpoints include: Mean change in BCVA from baseline to Month 24; mean change in CRT from baseline to Month 24; mean number of IVT-AFL injections by Month 24; maintenance of vision at Months 24

Depending on the country, patients were treated following either the

Treatment-naïve patients with nAMD (aged ≥50 years)

EMA label: After three initial monthly injections, minimum interval of 8 weeks in Year 1

or

Non-EMA label: After three initial monthly injections, minimum interval of 4 weeks in Year 1

IVT-AFL treatment intervals could be extended according to local protocols[a]

Decision to treat with an IVT-AFL proactive regimen (fixed dosing or T&E) made by the investigator prior to enrollment. [a]Treatment intervals could be extended in 2- to 4-week increments up to a maximum of 12 or 16 weeks according to the local label.

BCVA, best-corrected visual acuity; **CRT**, central retinal thickness; **EMA,** European Medicines Agency; **ETDRS,** Early Treatment Diabetic Retinopathy Study.

Patient baseline demographics

	EMA label-aligned (n=1165)	Non-EMA label-aligned (n=301)	Total (N=1466)
Country (n)	UK (n=496) France (n=147) South Korea (n=100) Belgium (n=81) Spain (69) 9 countries (n=<50)[a]	Canada (n=190) Australia (n=60) Switzerland (n=51)	
Age, years	**78.3** ±8.6	**80.2** ±8.3	**78.7** ±8.5
Female, n (%)	705 (61)	186 (62)	891 (61)
Mean BVCA, ETDRS letters[b]	**55.1** ±19.8	**51.6** ±21.8	**54.3** ± 20.3
Mean CRT, µm[c]	**378** ±131	**362** ±107	**374** ±126
BCVA letter score category, n (%)			
<35	139 (11.9)	46 (15.3)	185 (12.6)
≥35 to <70	692 (59.4)	177 (58.8)	869 (59.3)
≥70	334 (28.7)	78 (25.9)	412 (28.1)
Primary intended treatment regimen after initial monthly injections			
Proactive T&E	999 (85.8)	284 (94.4)	1283 (87.5)
Proactive fixed treatment	166 (14.2)	17 (5.6)	183 (12.5)

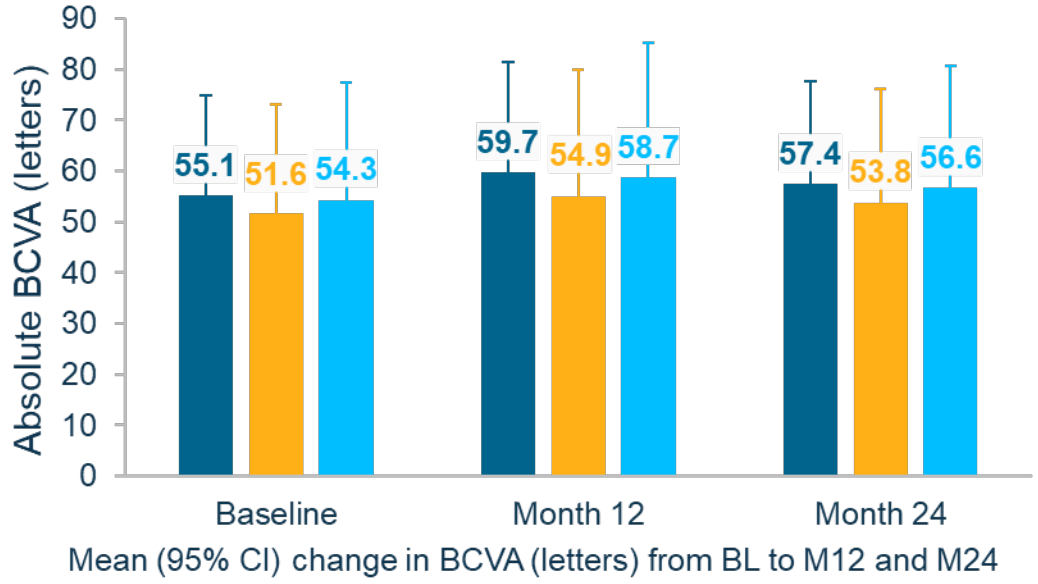
Of the 1561 patients enrolled in the XTEND study, **1466 patients comprised the FAS at 2 years**

In total, 393 patients discontinued treatment, including 82 patients who were lost to follow-up

FAS. Mean ±SD unless otherwise stated. [a]Argentina, Colombia, Denmark, Ireland, Italy, Mainland China, Norway, Sweden, and Thailand. [b]ETDRS and Snellen chart with conversion to ETDRS were recommend to measure BCVA.[c]Spectral-domain and time-domain optical coherence tomography were used to measure CRT and results were interpreted at local sites.
FAS, full analysis set.

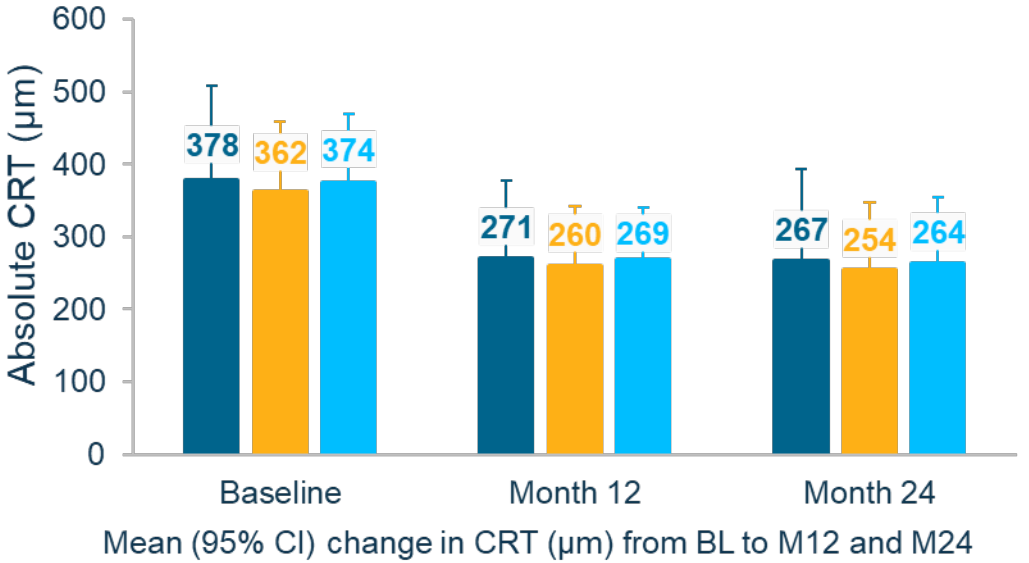
Change in BCVA and CRT from baseline to Month 24

EMA label
Non-EMA label
Total



Mean (95% CI) change in BCVA (letters) from BL to M12 and M24

	EMA label (n=1165)	Non-EMA label (n=301)	Total (N=1466)
M12	**4.6** (3.6, 5.6)	**3.4** (1.5, 5.2)	**4.3** (3.4, 5.3)
M24	**2.3** (1.2, 3.4)	**2.2** (0.1, 4.3)	**2.3** (1.3, 3.3)



Mean (95% CI) change in CRT (µm) from BL to M12 and M24

	EMA label (n=894[a])	Non-EMA label (n=273[a])	Total (N=1167[a])
M12	**–107** (–116, –98)	**–103** (–118, –86)	**–106** (–114, –99)
M24	**–109** (–118, –110)	**–109** (–123, –96)	**–109** (–117, –102)

Similar improvements were reported in patients, regardless of the label type

FAS, LOCF. Data are mean ±SD unless otherwise stated. Error bars denote SD. [a]N numbers differ between change in CRT from BL to M12 and M24 and absolute CRT at M12 and M24 as some patients did not have BL CRT values.

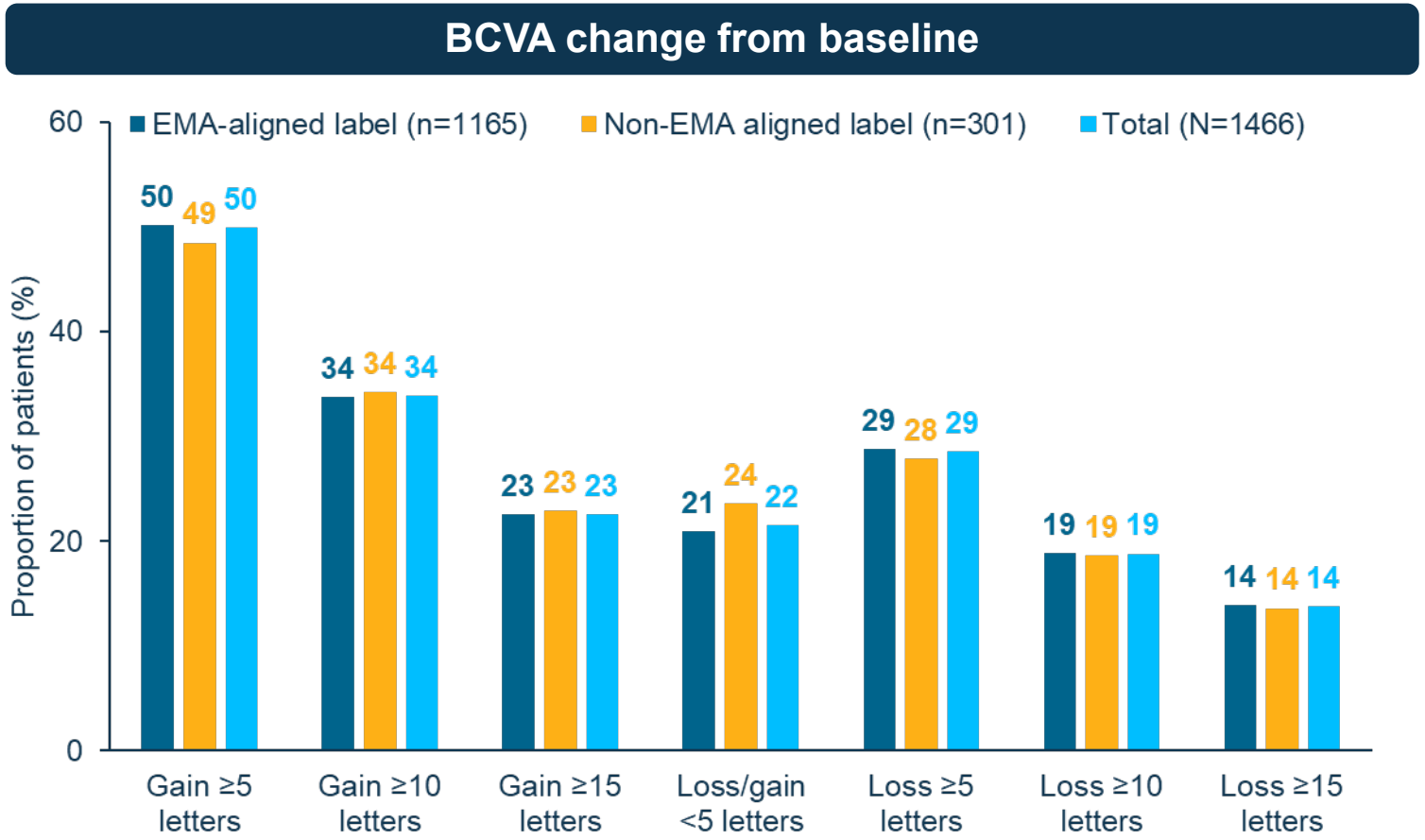
BL, baseline; **CRT,** central retinal thickness; **LOCF**, last observation carried forward; **M,** month.

Visual outcomes at 24 months

50% of patients **gained ≥5 letters** at 24 months

23% of patients **gained ≥15 letters** at 24 months

86% of patients **maintained vision (lost <15 letters)** at 24 months

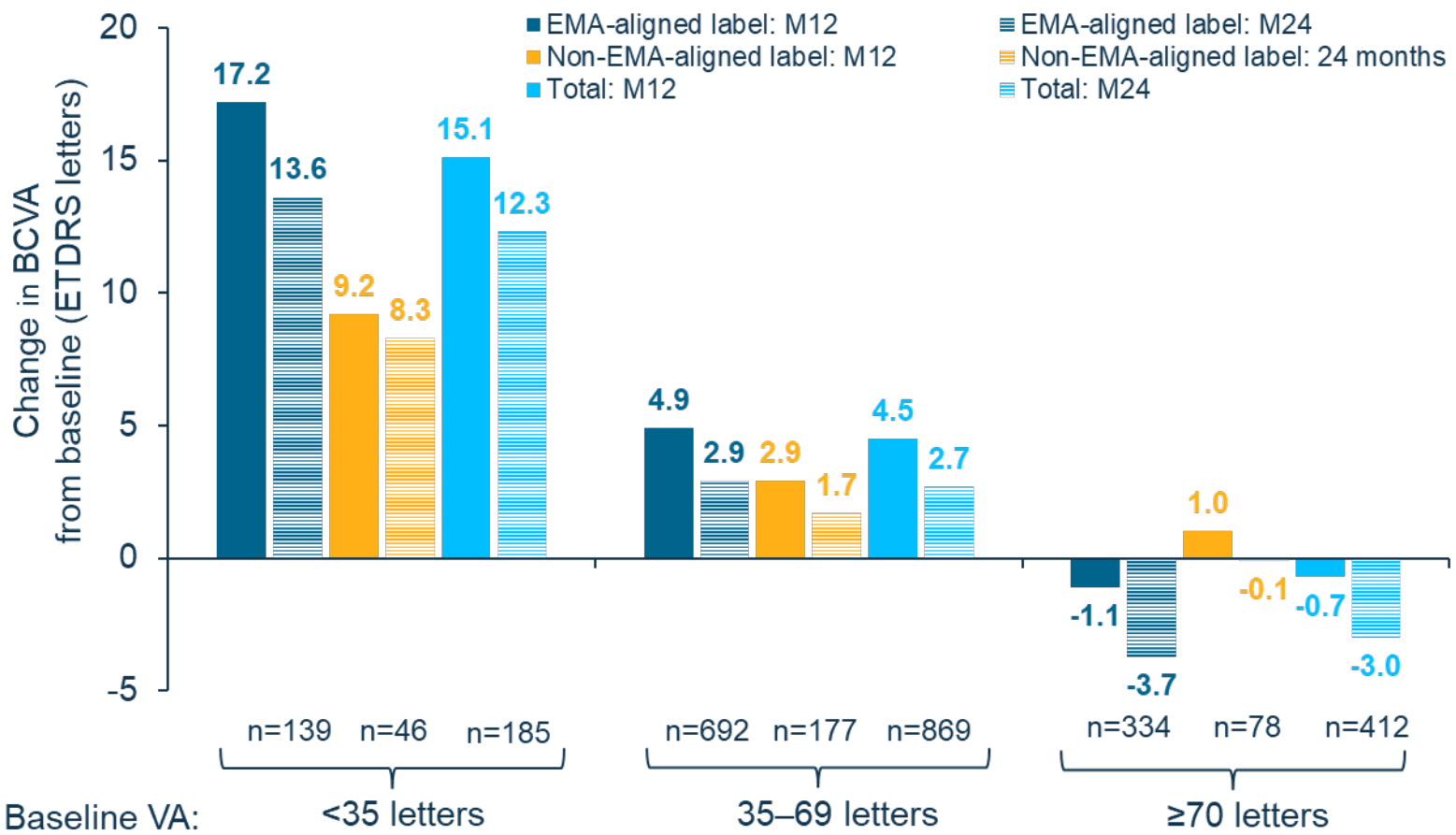


FAS, LOCF.

Visual outcomes at 24 months

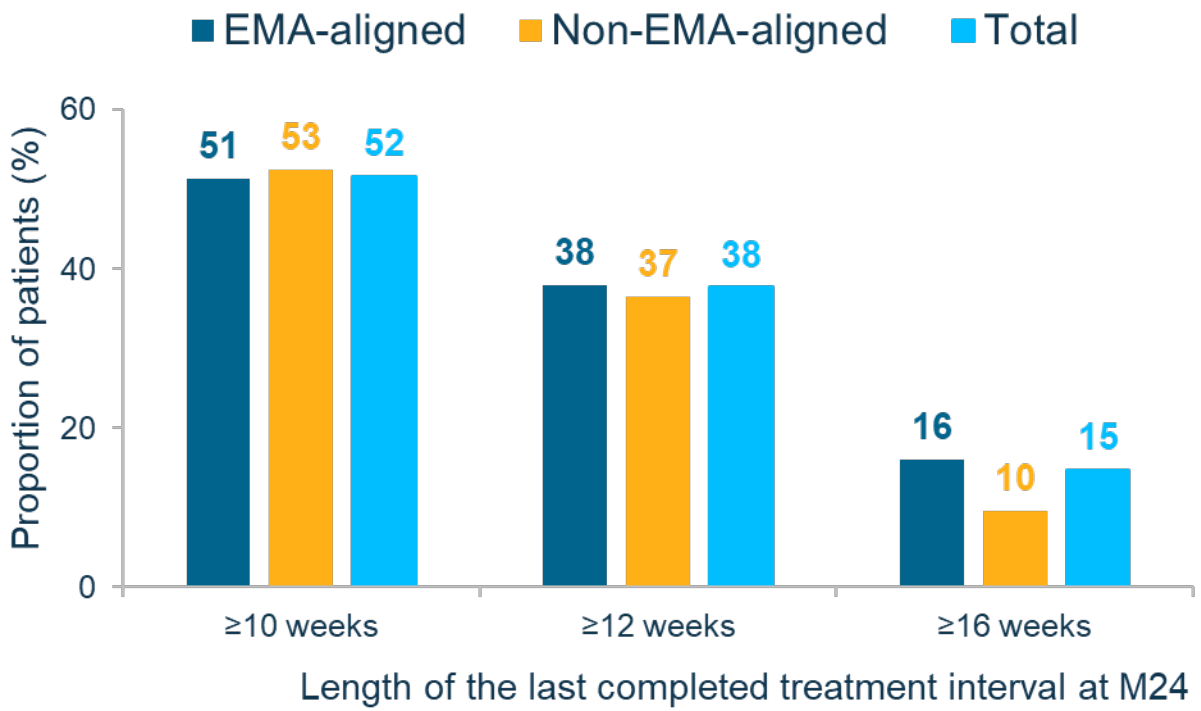
- Mean BCVA change at Months 12 and 24 was **highest in patients with a baseline BCVA of <35 letters**
- In patients with a baseline VA of ≥70 letters, BCVA was **maintained ≥70 letters**
- The proportion of patients with ≥70 letters increased from 28% at baseline to 42% at M24

Mean change in BCVA over 24 months stratified by baseline visual acuity



FAS, LOCF.
VA, visual acuity.

Treatment exposure



Mean ±SD number of injections from BL to M12 and M24[a]

	EMA label (n=1165)	Non-EMA label (n=301)	Total (N=1466)
M12	**7.4** ±2.6	**8.6** ±2.8	**7.7** ±2.7
M24	**10.5** ±4.9	**12.0** ±5.2	**10.8** ±5.0

The majority of IVT-AFL injections were received by M12, with a mean of 3.1 injections from M12 to M24 in the overall cohort

Most patients (88%) were scheduled to be treated according to a T&E dosing regimen

Planned treatment interval extensions were capped in some countries due to the COVID-19 pandemic[b]

Change in BCVA[c] and CRT[d] from baseline to M24 and injection number[e] were comparable in 'pre-COVID' and 'during COVID' groups

Mean±SD time in study (defined as days between first injection and last visit documented) was **20.0±5.9 months**

[a]Injections up to 420 days (12 months). [b]The COVID-19 pandemic began after study initiation (First Patient First Visit: May 15, 2019). National guidance during the pandemic was a strong modulator of treatment interval extension. Fixed treatment intervals of 8 weeks in the UK, and the minimum effective interval in France, were recommended. [c]Mean [95% CI] BCVA change from BL to M24 in the 'pre-COVID' (n= 271) and 'during COVID' (n=1195) group were +1.7 [−0.3, 3.6] letters and +2.4 [1.3, 3.6] letters respectively. [d]Mean ±SD CRT change at M24 in the 'pre-COVID' (n= 179) and 'during COVID' group (n=949) were −107 ±123 µm and −109 ±132 µm respectively. [e]Mean number of injections at M24 for the 'pre-COVID' (n= 271) and 'during COVID' (n=1195) were 10.9±4.8 and 10.9±5.0, respectively. **COVID-19,** Coronavirus Disease 2019.

Safety summary

Number of patients (%)	EMA label (n=1221)	Non-EMA label (n=329)	Total (N=1550)
Any TEAEs	**384 (31)**	**80 (24)**	**464 (30)**
Any ocular	271 (22)	54 (16)	325 (21)
Any non-ocular	178 (15)	38 (12)	216 (14)
Any serious TEAEs	**133 (11)**	**23 (7)**	**156 (10)**
Any serious ocular	39 (3)	2 (<1)	41 (3)
Any serious non-ocular	97 (8)	22 (7)	119 (8)
Any serious drug-related TEAEs	**12 (1)**	**1 (<1)**	**13 (<1)**
Any serious drug-related ocular[a]	8 (<1)	0	8 (<1)
Any serious drug-related non-ocular	4 (<1)	1 (<1)	5 (<1)

For the total population for both eyes, 17 (1%) cases of IOI were reported, including three cases of endophthalmitis and one case of bacterial endophthalmitis[b] in study eyes

No cases of retinal vasculitis, retinal occlusive vasculitis, or retinal artery occlusion were reported

No new ocular safety concerns were identified

[a]Serious drug-related ocular TEAEs: Anterior chamber inflammation, bacterial endophthalmitis, injection site inflammation, lid sulcus deepened, retinal pigment epithelial tear and rhegmatogenous retinal detachment (all n=1), and endophthalmitis (n=2). [b]Per 15,875 injections in the study eye (approximately one case per 5292 patients).
IOI, intraocular inflammation; **TEAE,** treatment-emergent adverse event.

Conclusions

Treatment-naïve patients with nAMD proactively treated with either IVT-AFL label type achieved **clinically relevant improvements in BCVA and CRT** and **extended treatment intervals** after **24 months**

Functional and anatomic improvements were achieved within the first 12 months of treatment and were generally maintained across 24 months even in the setting of the COVID pandemic

The safety profile of IVT-AFL was consistent with previous studies, and no cases of retinal vasculitis, retinal occlusive vasculitis, or retinal artery occlusion were reported

The study is ongoing, with the **36-month analysis** planned for 2024

Thank you to all XTEND patients and investigators

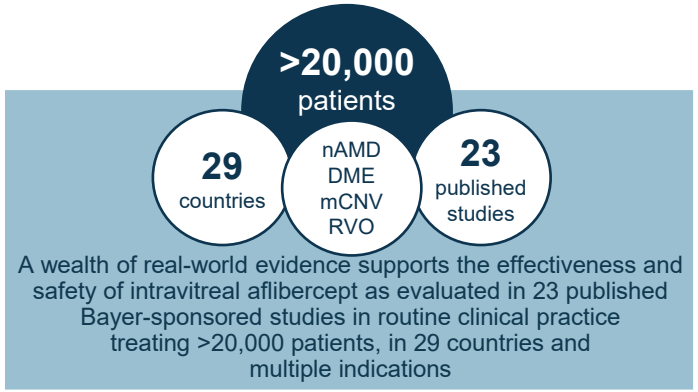
For more information, please contact:

Clare Bailey
Clare.Bailey@uhbw.nhs.uk

Acknowledgments

The XTEND study was sponsored by Bayer AG, Leverkusen, Germany. Medical writing support, under the direction of the authors, was provided by ApotheCom and funded by Bayer Consumer Care AG, Basel, Switzerland, in accordance with Good Publication Practice (GPP) guidance (*Ann Intern Med.* 2022;175:1298–1304).

XTEND is part of the aflibercept RWE program:



A wealth of real-world evidence supports the effectiveness and safety of intravitreal aflibercept as evaluated in 23 published Bayer-sponsored studies in routine clinical practice treating >20,000 patients, in 29 countries and multiple indications

World map showing XTEND study site countries only.