The XTEND study: 3-year results from a global observational study investigating proactive dosing regimens with intravitreal aflibercept 2 mg in neovascular age-related macular degeneration in routine clinical practice

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Presented at the 24th European Society of Retina Specialists (EURETINA) Congress, Barcelona, Spain, September 19–22, 2024

Disclosures

Disclosures: Presenting author

Clare Bailey: Honoraria/advisory board meetings for Alimera Sciences, Apellis, Bayer, Boehringer Ingelheim, Janssen, Novartis, and Roche.

Disclosures: Co-author group

VC: Grants from Bayer, Novartis, and Roche; advisory board member for Alcon Laboratories, Appelis, Bayer, Boehringer Ingelheim, Novartis, and Roche. **PM**: Consultant for Allergan Inc., Apellis, Bayer, Novartis, and Roche; lecture honoraria for Bayer; support for attending meetings and/or travel from Bayer, and Roche; and member of a data safety monitoring board or advisory board for Apellis and Bayer. **SWK**: Personal fees and non-financial support from Bayer Korea. **HA** and **XZ**: Employees of Bayer Consumer Care AG, Basel, Switzerland. **TM**: Employee of Bayer AG, Berlin, Germany. **J-FK**: Consultant for AbbVie, Apellis, Bayer, Eyepoint Pharma, Ocuphire, Roche, Théa Pharmaceuticals, and Carl Zeiss Meditec AG; member of a data safety monitoring board or advisory board for Alexion, Novo Nordisk, and Opthea.

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] was a 36-month, multicenter, observational, prospective study that recruited patients from 127 sites in 17 countries[1]

The **XTEND study** examined treatment outcomes of **real-world proactive IVT-AFL 2 mg treatment regimens** (fixed dosing or T&E) in treatment-naïve patients with nAMD in routine clinical practice[1]

This analysis presents the **3-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. This study was initiated in May 2019 and data collection concluded in October 2023. **IVT-AFL**, intravitreal aflibercept; **nAMD**, neovascular age-related macular degeneration; **T&E**, treat-and-extend; **VEGF**, vascular endothelial growth factor.

1. Korobelnik JF, et al. *Ophthalmol Ther* 2024;13:725–738.

XTEND (NCT03939767) observational, prospective study design

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

Secondary endpoints included: Mean change in BCVA from baseline to 24 and 36 months; mean change in CST from baseline to 12, 24, and 36 months; mean number of IVT-AFL injections by 12, 24, and 36 months; proportion of patients maintaining vision[a] at 12, 24, and 36 months

Depending on the country, patients were treated with IVT-AFL 2 mg following either the:

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

EMA-aligned label: After 3 initial monthly injections, minimum interval of 8 weeks in Year 1

or

Non-EMA-aligned label: After 3 initial monthly injections, minimum interval of 4 weeks in Year 1

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

Decision to treat with an IVT-AFL proactive regimen (fixed dosing or T&E) made by the investigator prior to enrollment. [a]Maintenance of vision defined as losing <15 visual acuity score letters since baseline; [b]Treatment intervals could be extended in 2-week to 4-week increments up to a maximum of 12 or 16 weeks according to the local label.

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

Baseline demographics and ocular characteristics

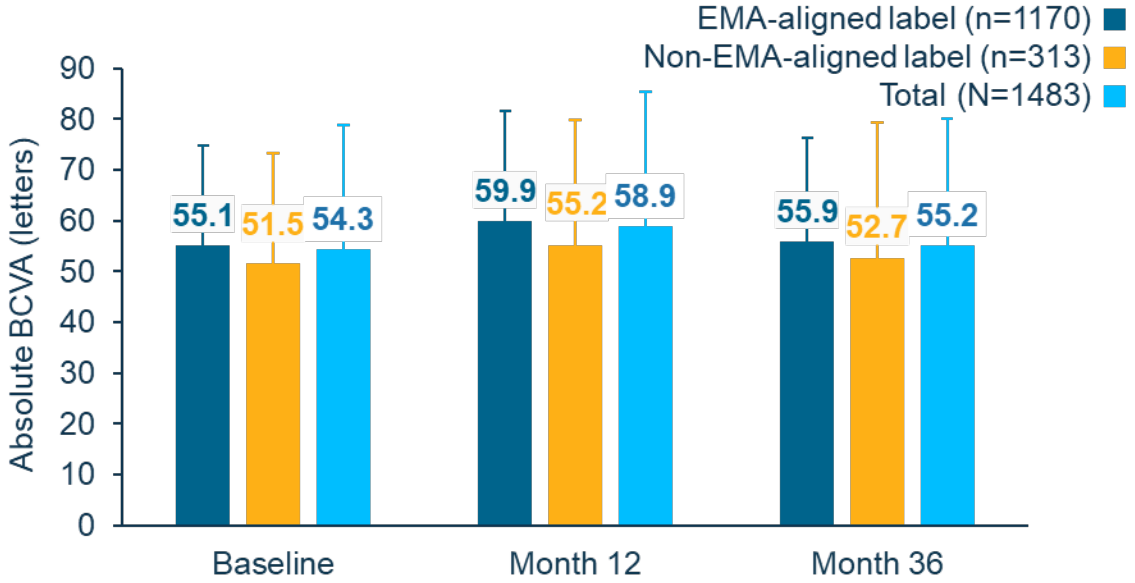
	EMA-aligned label (n=1170)	Non-EMA-aligned label (n=313)	Total (N=1483)
Country (n)	UK (n=497) France (n=149) South Korea (n=100) Belgium (n=81) Spain (n=69) 9 countries[a] (n≤50)	Canada (n=190) Australia (n=72) Switzerland (n=51)	
Age, years	**78.4** ±8.5	**80.3** ±8.3	**78.8** ±8.5
Female, n (%)	707 (60)	189 (60)	896 (60)
Mean BVCA, ETDRS letters[b]	**55.1** ±19.8	**51.5** ±21.7	**54.3** ±20.3
Mean CST, µm[c]	**377** ±130	**366** ±110	**375** ±125
BCVA letter score category, n (%) <35 ≥35 to <70 ≥70	 137 (12) 697 (60) 336 (29)	 48 (15) 186 (59) 79 (25)	 185 (12) 883 (60) 415 (28)
Primary intended treatment regimen after initial monthly injections, n (%) Proactive T&E Proactive fixed treatment	 1001 (86) 169 (14)	 296 (95) 17 (5)	 1297 (87) 186 (13)

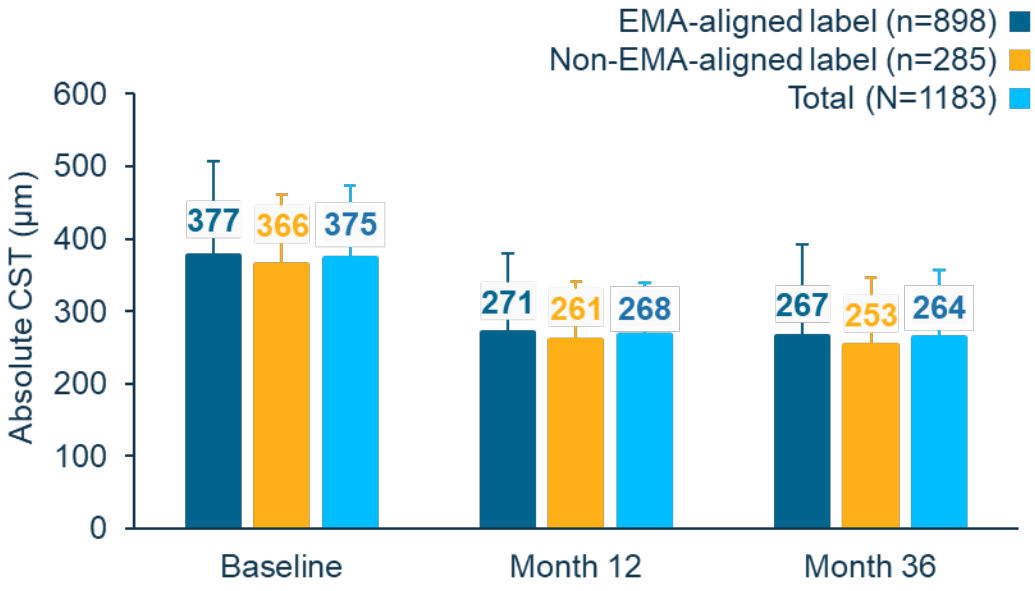
Of the 1561 patients enrolled in the XTEND study, **1483 patients comprised the FAS**

In total, 648 patients discontinued treatment, including 205 patients who were lost to follow-up

FAS. Mean ±SD unless otherwise stated. The final 36-month dataset has been used throughout so data may differ from previously presented 12-month and 24-month data. [a]Argentina, Colombia, Denmark, Ireland, Italy, Mainland China, Norway, Sweden, and Thailand; [b]ETDRS and Snellen chart with conversion to ETDRS were recommended to measure BCVA; [c]Spectral-domain and time-domain optical coherence tomography were used to measure CST, and results were interpreted at local sites. **FAS**, full analysis set; **SD**, standard deviation.

Change in BCVA and CST from baseline to Month 36





Mean (95% CI) change in BCVA (letters) from baseline to M12 and M36

	EMA-aligned label (n=1170)	Non-EMA-aligned label (n=313)	Total (N=1483)
M12	**4.8** (3.8, 5.8)	**3.7** (1.9, 5.5)	**4.6** (3.7, 5.4)
M36	**0.8** (–0.5, 2.0)	**1.2** (–1.0, 3.4)	**0.9** (–0.2, 1.9)

Mean (95% CI) change in CST (µm) from baseline to M12 and M36

	EMA-aligned label (n=832[a])	Non-EMA-aligned label (n=278[a])	Total (N=1110[a])
M12	**–107** (–116, –98)	**–104** (–119, –90)	**–106** (–114, –99)
M36	**–110** (–119, –101)	**–112** (–125, –98)	**–110** (–118, –103)

Similar functional and anatomic outcomes at each time point were reported for patients regardless of which treatment regimen they received per label type

FAS, LOCF. Error bars denote SD. [a]N numbers differ between absolute CST at M12 and M36 and change in CST from baseline to M12 and M36 because some patients did not have baseline CST values.
CI, confidence interval; **LOCF**, last observation carried forward; **M**, month.

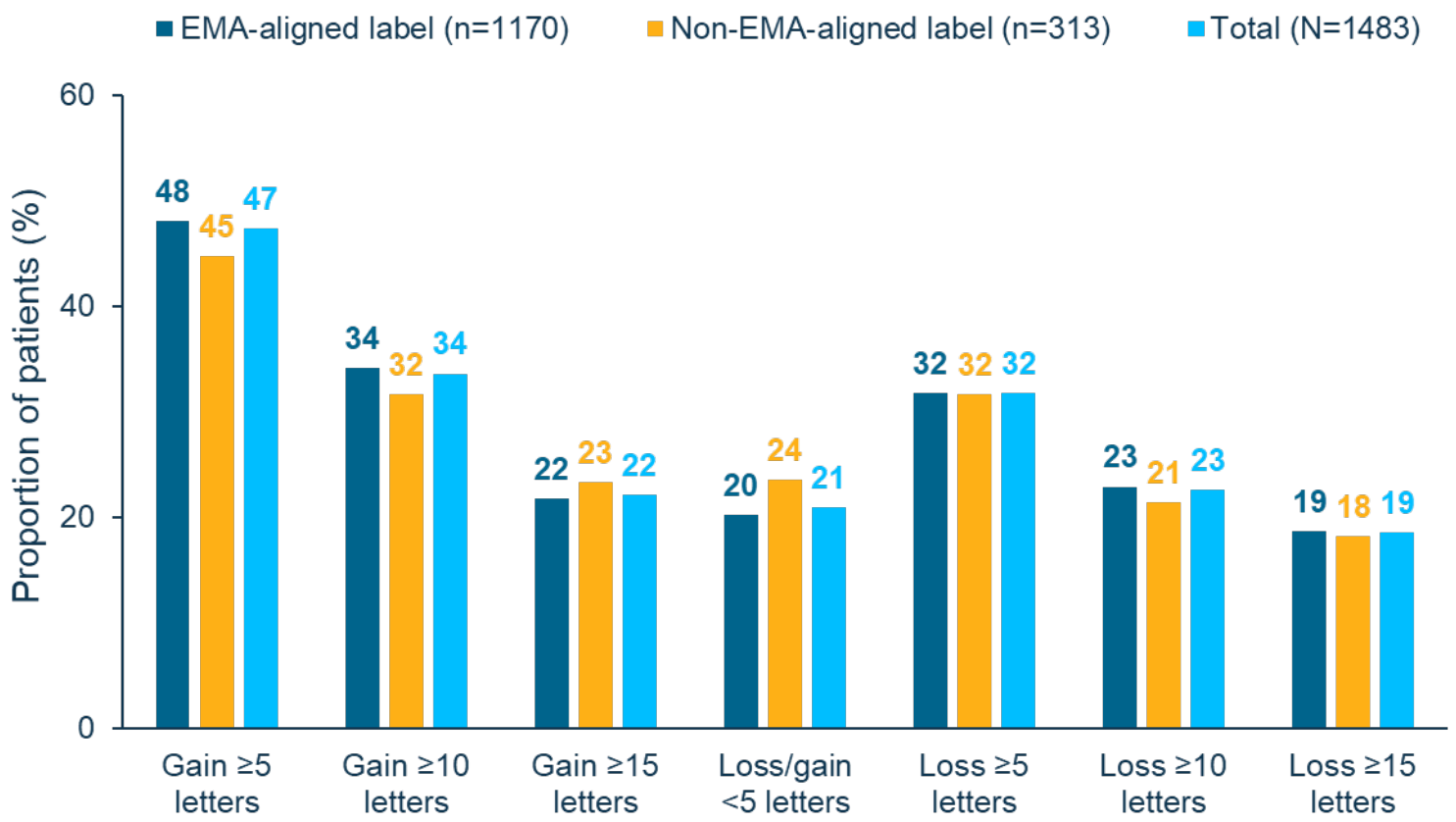
Visual outcomes at Month 36

47% of patients **gained ≥5 letters** at 36 months

22% of patients **gained ≥15 letters** at 36 months

81% of patients **gained or maintained vision (lost <15 letters)** at 36 months

BCVA change from baseline to Month 36

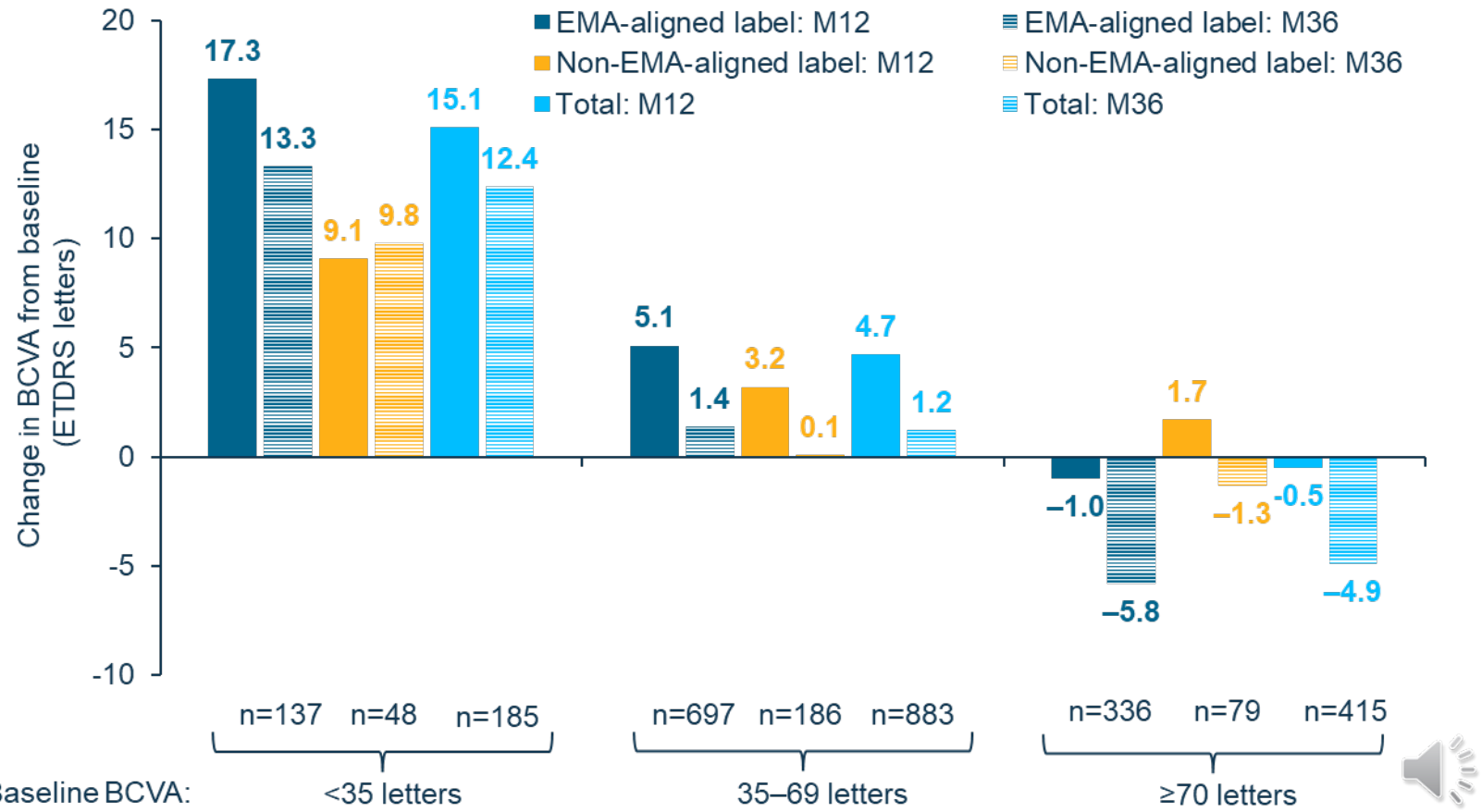


FAS, LOCF.

Visual outcomes at Month 36

- Mean BCVA change at 12 and 36 months was **highest in patients with a baseline BCVA of <35 letters**
- In patients with a baseline BCVA of **≥70 letters**, BCVA was **maintained at ≥70 letters** in the total population[a]
- The proportion of patients with **≥70 letters** increased from **28% at baseline to 40% at 36 months**

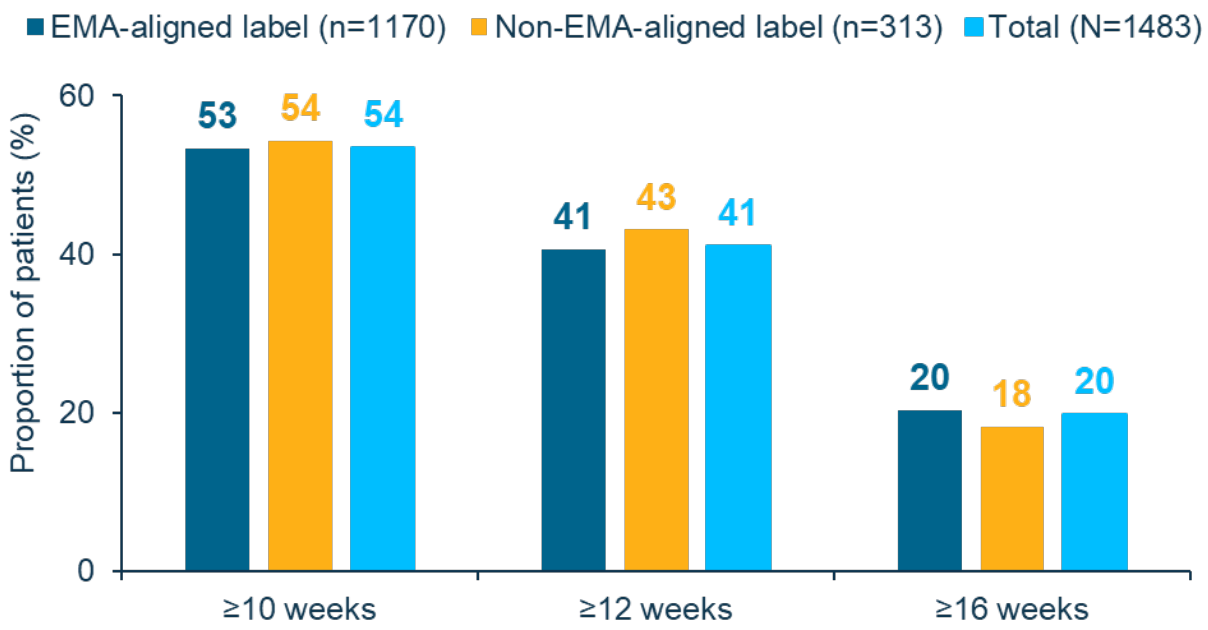
Mean change in BCVA over 36 months stratified by baseline BCVA



FAS, LOCF. [a]Mean ±SD BCVA at M36 was 69.2 ±18.0 letters and 73.8 ±9.3 letters in the EMA-aligned label and non-EMA-aligned label, respectively. In the total population, the mean ±SD BCVA at M36 was 70.1 ±16.8 letters.

Treatment exposure

Length of the last completed treatment interval at Month 36



Mean ±SD number of injections from baseline to M12 and M36[a]

	EMA-aligned label (n=1170)	Non-EMA-aligned label (n=313)	Total (N=1483)
M12	**7.4** ±2.6	**8.6** ±2.8	**7.7** ±2.7
M36	**13.3** ±7.4	**15.4** ±7.7	**13.7** ±7.5
	Total number of IVT-AFL 2 mg injections		
Year 2	3.5	4.0	3.6
Year 3	2.4	2.8	2.4

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

Change in BCVA from baseline to M36 was numerically higher in the "during COVID-19" group than the "pre-COVID-19" group[c]

Change in CST[d] from baseline to M36 and injection number[e] were comparable in "pre-COVID-19" and "during COVID-19" groups

Mean ±SD time in study (defined as days between first injection and last visit documented) was **29.2 ±10.4 months**

[a]Injections up to 420 days (12 months) and 1140 days (36 months); [b]The "pre-COVID-19" group included all patients who received their regular end-of-observation visit before the start date of the COVID-19 pandemic or who received their first injection 180 days prior to their country of residence's COVID-19 start date. The pandemic start date (between February and March 2020) was provided by Bayer representatives based on individual national guidelines. The "during COVID-19" group included all other patients; [c]Mean (95% CI) BCVA change from baseline to M36 in the "pre-COVID-19" (n=272) and "during COVID-19" (n=1211) group were −0.5 (−2.8, 1.7) letters and +1.2 (−0.1, 2.4) letters, respectively; [d]Mean ±SD CST change at M36 in the "pre-COVID-19" (n=183) and "during COVID-19" group (n=961) were −110 ±123 µm and −109 ±133 µm, respectively; [e]Mean ±SD number of injections at M36 for the "pre-COVID-19" (n=272) and "during COVID-19" (n=1211) were 13.7 ±7.2 and 13.9 ±7.6, respectively. **COVID-19**, coronavirus disease 2019.

Safety summary

Number of patients, n (%)	EMA-aligned label (n=1219)		Non-EMA-aligned label (n=329)		Total (N=1548)	
Any TEAEs	**610**	**(50)**	**114**	**(35)**	**724**	**(47)**
Any ocular	488	(40)	80	(24)	568	(37)
Any non-ocular	246	(20)	54	(16)	300	(19)
Any serious TEAEs	**245**	**(20)**	**33**	**(10)**	**278**	**(18)**
Any serious ocular	113	(9)	7	(2)	120	(8)
Any serious non-ocular	144	(12)	29	(9)	173	(11)
Any serious drug-related TEAEs	**23**	**(2)**	**2**	**(1)**	**25**	**(2)**
Any serious drug-related ocular[a]	18	(1)	1	(<1)	19	(1)
Any serious drug-related non-ocular	5	(<1)	1	(<1)	6	(<1)

In the total population for both eyes, 26 cases of IOI were reported, including 6 cases of endophthalmitis. One case of bacterial endophthalmitis occurred in the study eyes[b]

No cases of retinal vasculitis, retinal occlusive vasculitis, or retinal artery occlusion were reported. One case of retinal vascular disorder was reported

No new ocular safety signals were identified

[a]Serious drug-related ocular TEAEs: Anterior chamber inflammation, bacterial endophthalmitis, cataract, cataract traumatic, detachment of retinal pigment epithelium, eye inflammation, injection-site inflammation, injection-site infection, retinal hemorrhage, retinal edema, and rhegmatogenous retinal detachment (all n=1), nAMD (n=2), endophthalmitis and retinal pigment epithelial tear (both n=4);
[b]Per 20,370 injections in the study eye. **IOI**, intraocular inflammation; **TEAE**, treatment-emergent adverse event.

Conclusions

Treatment-naïve patients with nAMD proactively treated with the EMA-aligned label or the non-EMA-aligned label type achieved **meaningful improvements in BCVA and CST** throughout the XTEND study and **extended treatment intervals** at **36 months**

Functional and anatomic improvements were achieved within the first 12 months of treatment and were consistent in those following either label, even in the setting of the COVID-19 pandemic

Patients received the majority of IVT-AFL 2 mg injections in the first 12 months and vision was generally maintained over 36 months from baseline, suggesting that **long-term maintenance of vision is achievable with IVT-AFL 2 mg in patients with nAMD**

The safety profile of IVT-AFL 2 mg at 36 months was consistent with previous studies[1,2] and that observed up to 24 months in XTEND.[3] No cases of retinal vasculitis, retinal occlusive vasculitis, or retinal artery occlusion were reported

1. Heier JS, et al. *Ophthalmology* 2012;119:2537–2548. 2. Schmidt-Erfurth U, et al. *Ophthalmology* 2014;121:193–201. 3. Korobelnik JF, et al. *Ophthalmol Ther* 2024;13:725–738.

Thank you to all XTEND patients and investigators

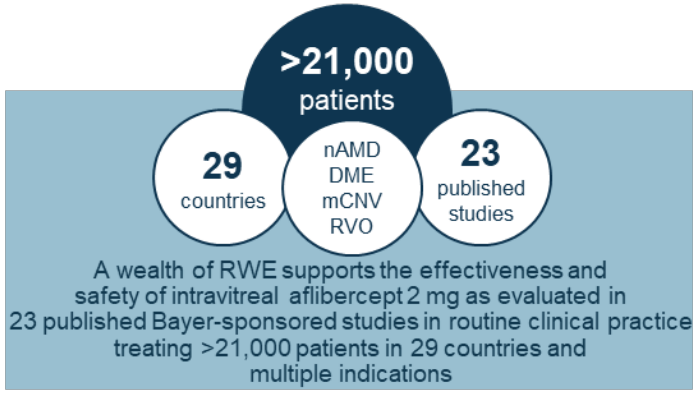
Acknowledgments

The authors would like to posthumously acknowledge Ramin Tadayoni for his involvement in the XTEND study and the EURETINA 2024 abstract development.

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).

Project management and administrative support for the XTEND study were provided by JinKyung Lee and Marcel Schulze (Bayer AG, Berlin, Germany).

XTEND[1] is part of the aflibercept RWE program:



A wealth of RWE supports the effectiveness and safety of intravitreal aflibercept 2 mg as evaluated in 23 published Bayer-sponsored studies in routine clinical practice treating >21,000 patients in 29 countries and multiple indications

World map showing XTEND study-site countries only.
DME, diabetic macular edema; **mCNV**, myopic choroidal neovascularization; **RVO**, retinal vein occlusion.

1. Korobelnik JF, et al. *Ophthalmol Ther* 2024;13:725–738.