A Non-interventional Study of Real-World Proactive Treatment Regimens with Aflibercept in Patients with nAMD: XTEND Study UK Cohort Year 1 Primary Analysis

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INTRODUCTION

Treat & extend (T&E) is a proactive, individualised treatment regimen aiming to minimise the risk of disease recurrence, with the goal of maintaining visual acuity gains, while reducing the treatment burden associated with anti-VEGF therapy.

XTEND (NCT03939767) is an ongoing, 36-month, prospective study examining treatment outcomes of real-world proactive intravitreal aflibercept (IVT-AFL) regimens (fixed dosing or T&E) in patients with neovascular age-related macular degeneration (nAMD).

XTEND is recruiting patients from 127 sites in 17 countries. The Year 1 primary analysis for the UK cohort is described here.

METHODS

Treatment-naïve patients aged ≥50 years with nAMD for whom the decision to treat with an IVT-AFL proactive regimen had already been made, were eligible for inclusion.

Following three initial monthly injections, the minimum treatment interval was expected to be 8 weeks during Year 1, as per label requirements. According to the label, intervals could be extended in 2- or 4-weekly increments up to 16 weeks.

Primary endpoint was mean change in best-corrected visual acuity (BCVA) from baseline to Month 12 (M12). Secondary endpoints included anatomic parameters and injection numbers/treatment intervals. Safety was assessed throughout; statistics are descriptive.

RESULTS

Patient demographics

The global full analysis set (FAS) included 1430 patients.

The UK cohort FAS included 489 patients (mean±SD age: 79.7±8.1 years; 64% female), representing 34% of the total global 12-month dataset **(Table 1)**.

At baseline, 111 patients were intended to receive a fixed dosing regimen, and 378 were intended to receive the treat & extend regimen **(Table 1)**.

RESULTS

Functional and anatomic outcomes

From a mean±SD baseline BCVA of 55.3±15.7, mean (95% CI) change to M12 was +3.4 (1.9, 4.8) letters **(Figure 1)**.

Patients with a baseline BCVA <35 letters demonstrated the greatest BCVA gains (+9.4 letters), and vision was maintained above 70 letters in patients with baseline BCVA of ≥70 letters **(Figure 1)**.

From baseline (396±144µm) mean±SD change in central retinal thickness was −105±143µm **(Figure 2)**.

Treatment patterns

The COVID-19 pandemic began after study initiation, and planned treatment interval changes were influenced by local or Royal College of Ophthalmologists (RCOphth) COVID-19 clinical guidance.[1] Following this guidance, many UK study sites maintained patients on 8-weekly intervals during the pandemic.

The mean±SD number of IVT-AFL injections was 7.0±2.2 by M12 **(Figure 3)**.

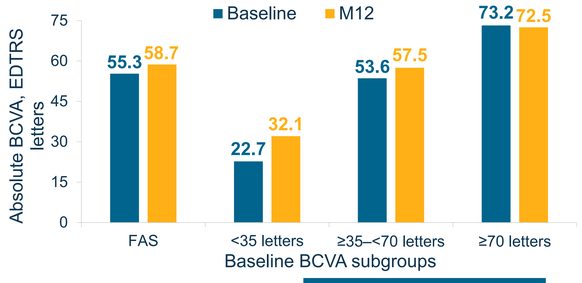
Despite the potential impact of the COVID-19 pandemic, last completed injection intervals were ≥10 weeks in 36% patients, ≥12 weeks for 24% of patients, and ≥16 weeks for 9% of patients **(Figure 3)**.

TABLE 1:
Patient demographics and baseline characteristics

	XTEND UK Cohort (N=489)
Age, years	**79.7**±8.1
Female, n (%)	314 **(64)**
VA, ETDRS letters	**55.3**±15.7
CRT, µm	**396**±144
Time from diagnosis to first IVT-AFL treatment, months	
Median (IQR)	**1.0** (1.0, 11.0)
Mean	**13.1**
Range	(1.0, 858.0)
Planned treatment regimen	
T&E, n (%)	378 **(77)**
Fixed dosing, n (%)	111 **(33)**

Data are mean ±SD unless otherwise indicated. CRT, central retinal thickness; IQR, inter-quartile range; SD, standard deviation; T&E, treat & extend; N/n, number; VA, visual acuity.

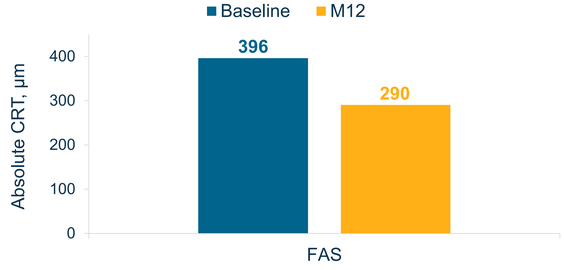
FIGURE 1:
Change in BCVA from baseline to M12



	Cohort (N=489)
Change in BCVA from baseline by M12 (mean±SD)	**3.4**±16.1
95% confidence interval	(1.9, 4.8)

<35 letters, n=44; ≥35–<70 letters, n=333; ≥70 letters, n=112
BCVA, best corrected visual acuity, FAS, full analysis data set; SD, standard deviation.

FIGURE 2:
Change in CRT from baseline to M12

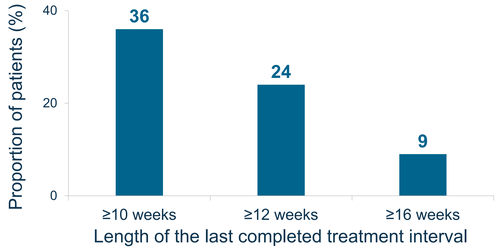


	Cohort (n=308)
Change in CRT from baseline by M12 (mean±SD)	**−105**±143µm
95% confidence interval	(−121, 89)

Absolute CRT baseline, n=339; absolute CRT M12, n=381; change from baseline to M12, n=308. N numbers differ as some patients did not have baseline CRT values. CRT, central retinal thickness; SD standard deviation

FIGURE 3:
Last completed treatment intervals

	Cohort (N=489)
Mean ±SD number of IVT-AFL injections	
From baseline **to M12**[a]	**7.0**±2.2



[a]Injections up to 420 days.

Safety

Among the serious treatment emergent adverse events, there were two cases of endophthalmitis (including one case of bacterial endophthalmitis) reported in study eyes **(Table 2)** and no new safety concerns were identified.

TABLE 2:
Safety outcomes by M12

Safety analysis set (n=518)	Patients, n (%)
Any TEAE	**104 (20.1)**
Ocular TEAEs	61 (11.8)
TEAEs related to study drug	12 (2.3)
Ocular TEAEs related to study drug[a]	10 (1.9)
Any serious TEAE	**37 (7.1)**
Serious ocular TEAEs	14 (2.7)
Serious TEAEs related to study drug[b]	5 (1.0)
TEAE-related deaths	1 (0.2)
Study drug discontinued due to TEAEs[c]	**7** (1.3)

[a]Most common: Cataract (n=2), and conjunctival haemorrhage (n=2). All other study-drug related ocular TEAEs occurred in 1 patient each. [b]One case each of bacterial endophthalmitis, cerebrovascular accident, endophthalmitis, retinal epithelial tear, and transient ischaemic attack. [c]Screened patients, n=535. TEAEs, treatment-emergent adverse events.

CONCLUSIONS

Treatment-naïve patients with nAMD in the UK proactively treated with IVT-AFL achieved robust vision gains at Year 1 in XTEND, despite the impact of the COVID-19 pandemic and its effect on planned treatment regimens. Improvements observed in the UK cohort are consistent with those observed across the global XTEND study.

The safety profile of IVT-AFL was consistent with previous studies[2,3] and no cases of retinal vasculitis were reported.

The study is ongoing, with the 24-month analysis planned for 2023.

References

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2. Eter et al. *Graefe's* 2021; 259(8): 2213–23
3. Weber et al. *BMC Ophthalmol* 2020;20(1):206

Disclosures

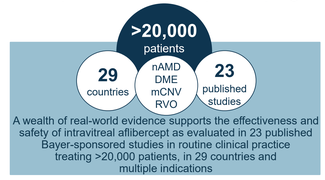
CB attended advisory board meetings for Bayer, Boehringer Ingelheim, Apellis, Novartis, Roche, Alimera Sciences, and Janssen, and has received lecture fees/travel support from Roche, Bayer, Novartis, Alimera Sciences. and Apellis; **MC** received consultancy fees from Roche, Novartis, and Bausch & Lomb, and received travel support from Novartis and Roche; **RG** received consultancy fees from Bayer, Novartis, Roche, and Boehringer Ingelheim; has attended advisory board meetings for Bayer, Novartis, Roche, and Biogen; and received lecture fees, research funding and travel grants from Bayer and Novartis; **NN** attended advisory board meetings and received lecture fees, research funding and travel grants from Bayer, Novartis, and Roche; **PP** received consultancy fees from Bayer, Roche, Boehringer Ingelheim and Novartis and received travel support, research grants, and lecture fees from Bayer; **JT** received meeting sponsorship and attended advisory boards for Bayer and Roche, and received research grants from Bayer, Roche, Boehringer Ingelheim, Gyroscope, and Janssen; **DV** has attended advisory board meetings for Bayer, Novartis, Roche, AbbVie, and TEVA; received lecture fees from Bayer, AbbVie, and Roche; has received research funding from Roche, Boehringer Ingelheim, and Alimera; and has received travel grants from Bayer, Roche, and Novartis; **HM, ZK, PM-W** are employees of Bayer Plc.

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