Baseline disease characteristics in patients maintaining q12 and q16 dosing with aflibercept 8 mg versus patients with shortened treatment intervals: A Phase 3 PULSAR post hoc analysis

Paolo Lanzetta,[1] Sergio Leal,[2] Tobias Machewitz,[3] Xin Zhang,[2] on behalf of the PULSAR study investigators

[1]Department of Medicine - Ophthalmology, University of Udine, and Istituto Europeo di Microchirurgia Oculare - IEMO, Udine-Milan, Italy; [2]Bayer Consumer Care AG, Basel, Switzerland; [3]Bayer AG, Berlin, Germany

2239 - C0192

PURPOSE

In the ongoing double-masked, 96-week, Phase 3 PULSAR trial in patients with treatment-naïve neovascular age-related macular degeneration (nAMD), 83% of patients receiving aflibercept 8 mg completed Week 48 on treatment intervals ≥12 weeks. This analysis describes baseline characteristics of patients maintained on their original randomized dosing regimens versus those whose intervals were shortened based on prespecified dose regimen modification criteria denoting disease activity.

METHODS

Patients were randomly assigned 1:1:1 to receive intravitreal aflibercept 8 mg every 12 (8q12) or 16 weeks (8q16) or aflibercept 2 mg every 8 weeks (2q8), each after three initial monthly injections.

In Year 1, from Week 16, treatment intervals could be shortened to a minimum of 8 weeks in the 8q12 or 8q16 groups if the patient met the dose regimen modification criteria (**Figure 1**).

The primary endpoint was change from baseline in best corrected visual acuity (BCVA) at Week 48.

RESULTS

The primary endpoint was met with aflibercept 8q12 vs 2q8 and 8q16 vs 2q8 (non-inferiority margin at 4 Early Treatment Diabetic Retinopathy Study [ETDRS] letters). **Figure 2** shows the mean absolute and arithmetic mean change from baseline to Week 48.

Overall, 79% of patients in the 8q12 group (n=316) maintained 12-week treatment intervals, and 77% of patients in the 8q16 group (n=312) maintained 16-week treatment intervals through Year 1 **(Figure 3)**.

Figures 4-6 show the baseline BCVA, central retinal thickness (CRT), and choroidal neovascularization (CNV) size of patients treated with aflibercept 8 mg in PULSAR maintained on their original randomized dosing regimens versus those whose intervals were shortened based on prespecified dose regimen modification criteria denoting disease activity. BCVA outcomes were similar across those who maintained on their original randomized dosing regimens versus those whose intervals were shortened for each baseline characteristic.

RESULTS

FIGURE 1: PULSAR: Dosing schedule and regimen modification in Year 1

	Day 1	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Wk 28	Wk 32	Wk 36	Wk 40	Wk 44	Wk 48
2q8	X	X	X		X	o	X	o	X	o	X	o	X
8q12	X	X	X		o	X	o	o	X	o	o	X	o
8q16	X	X	X		o	o	X	o	o	o	X	o	o

Stippled boxes = initial treatment phase; X = active injection; o = sham injections.

Note: Table does not reflect all dosing options once a patient's treatment interval is shortened.

DRM Criteria for Shortening Dosing Interval*

>5-letter loss in BCVA due to persistent or worsening nAMD

AND

>25-µm increase in CRT or new onset foveal neovascularization or foveal hemorrhage

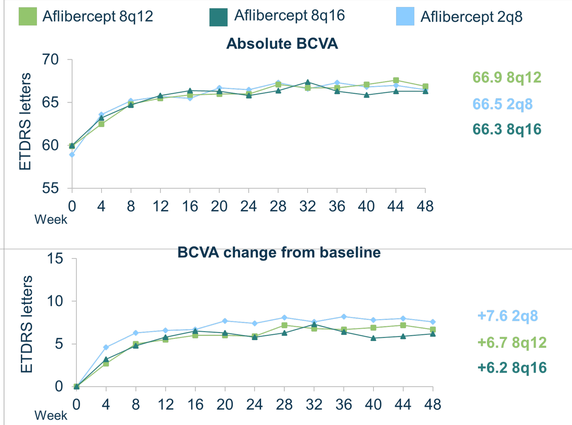
*All assessments compared to Week 12

DRM in Year 1

- Intervals can only be shortened → **Week 16 and 20:** Patients on 8q12 and 8q16 meeting DRM criteria shortened to q8
- Multiple opportunities to shorten interval → **Week 24:** Patients on 8q16 meeting DRM criteria shortened to q12
- Minimum interval for all patients was q8 → **Week 32 and 44 for 8q12 and Week 36[a] and 40 for 8q16:** Treatment interval shortened by 4 weeks for patients meeting DRM criteria

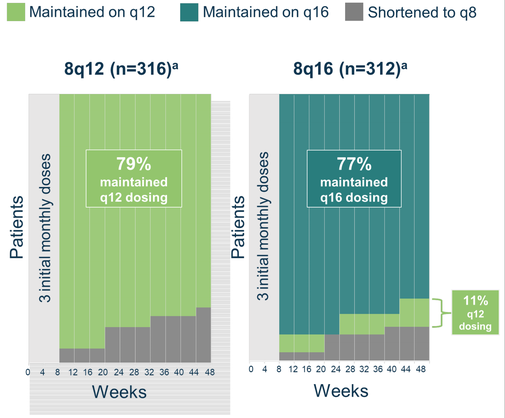
[a]At Week 36, patients on 8q16 who were previously shortened to q12 could have been shortened to q8.
BCVA, best corrected visual acuity; CRT, central retinal thickness; DRM, dose regimen modification; nAMD, neovascular age-related macular degeneration Wk, week.

FIGURE 2: BCVA outcomes: Mean absolute and mean change from baseline at Week 48



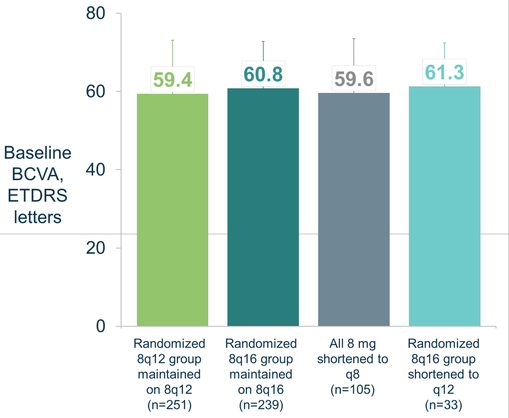
Observed values (censoring data post ICE); FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338 (at baseline). BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study. FAS, full analysis set; ICE, intercurrent events.

FIGURE 3: Proportions of patients maintaining q12- and q16-week intervals through Week 48



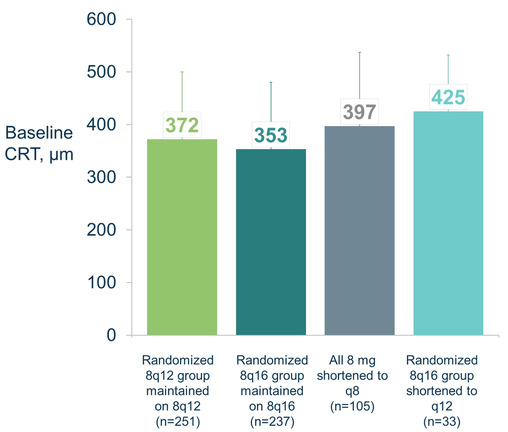
Patients shortened based on DRM assessments at some point through Week 48.
[a]Patients completing Week 48. DRM, dose modification regimen.

FIGURE 4: Patients who maintained or shortened dosing interval post-baseline: Mean baseline BCVA (ETDRS letters)



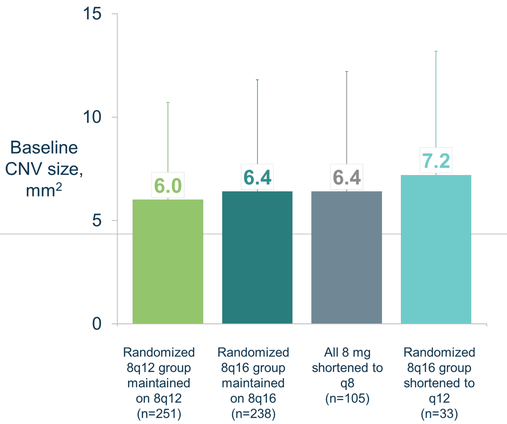
Error bars denote SD. BCVA, Best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

FIGURE 5: Patients who maintained or shortened dosing interval post-baseline: Mean baseline CRT (µm)



Error bars denote SD. CRT, central retinal thickness.

FIGURE 6: Patients who maintained or shortened dosing interval post-baseline: Mean baseline CNV size (mm^2)



Error bars denote SD. CNV, choroidal neovascularization.

CONCLUSIONS

The majority of patients with nAMD treated with intravitreal aflibercept 8 mg were maintained on q12 or q16 treatment intervals.

As BCVA, CRT, and CNV size were similar across groups that maintained 8q12 or 8q16 dosing, as well as to the group who had their interval shortened to q8, these baseline characteristics did not influence the treatment interval in nAMD.

The oral presentation **"Intravitreal aflibercept 8 mg injection in patients with neovascular age-related macular degeneration: 48-week results from the Phase 3 PULSAR trial"** will be presented by Prof Martin Spitzer in the AMD antiVEGF session on April 23, 2023 at 12:15–12:30 pm.

Disclosures

PL: Consultant for Aerie, Allergan, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, I-Care, Genentech, Novartis, Outlook Therapeutics, and Roche; **TM**: Employee of Bayer AG; **XZ** and **SL**: Employees of Bayer Consumer Care AG.

Acknowledgments

The PULSAR study was sponsored by Bayer AG (Leverkusen, Germany) and co-funded by Regeneron Pharmaceuticals, Inc (Tarrytown, NY, USA). The sponsor participated in the design and conduct of the study, analysis of the data, and preparation of this poster. 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) guidelines (*Ann Intern Med* 2022;175:1298–1304).

Scan the QR code to access all abstracts presented at ARVO 2023

Presented at The Association for Research in Vision and Ophthalmology (ARVO) 2023 Annual Meeting, New Orleans, LA, USA, April 23–27, 2023]