Subgroup analyses from the Phase 3 PULSAR trial of aflibercept 8 mg in patients with treatment-naïve neovascular age-related macular degeneration

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PURPOSE

The ongoing PULSAR (NCT04423718) study is a double-masked, 96-week, Phase 3 trial in patients aged ≥50 years with treatment-naïve neovascular age-related macular degeneration (nAMD). This subgroup analysis evaluated the treatment effects of aflibercept 8 mg versus 2 mg at Week 48 by baseline characteristics.

METHODS

Patients were randomly assigned 1:1:1 to receive intravitreal aflibercept 8 mg every 12 or 16 weeks (8q12, 8q16) or 2 mg every 8 weeks (2q8), each after three initial monthly injections. From Week 16, dosing intervals for aflibercept 8 mg were shortened if patients met prespecified dose regimen modification criteria denoting disease activity (**Figure 1**). The primary endpoint was change in best corrected visual acuity (BCVA) from baseline through Week 48. Subgroups were determined post hoc and subgroup analyses were exploratory. The analyzed subgroups comprised patients categorized by baseline BCVA, baseline central retinal thickness (CRT), choroidal neovascularization (CNV) type, and race.

RESULTS

Mean change in BCVA from baseline at Week 48 was numerically larger in patients with lower baseline BCVA (≤54 letters) and smaller in those with higher baseline BCVA (≥74 letters). Mean change and absolute BCVA letter scores at baseline and Week 48 were similar across the 8q12, 8q16, and 2q8 treatment groups (**Figure 2**).

In patients with baseline CRT <400 µm and ≥400 µm, mean BCVA from baseline to Week 48 in the 8q12, 8q16, and 2q8 treatment groups were also similar, resulting in similar absolute BCVA letter scores at Week 48 irrespective of treatment group (**Figure 3**).

Mean change in BCVA from baseline at Week 48 were also similar across all treatment groups in the patients with minimally classic, occult, and predominantly classic CNV (**Figure 4**).

Mean BCVA change and absolute letter scores at Week 48 were also similar in the 8q12, 8q16, and 2q8 treatment groups in the White and Asian patient populations in the PULSAR trial (**Figure 5**).

The proportions of White and Asian patients maintaining 8q12 and 8q16 dosing intervals up to Week 48 were comparable to the overall PULSAR population (**Figure 6**). Data are not reported for Black or African American patients due to small sample size (n=2).

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

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

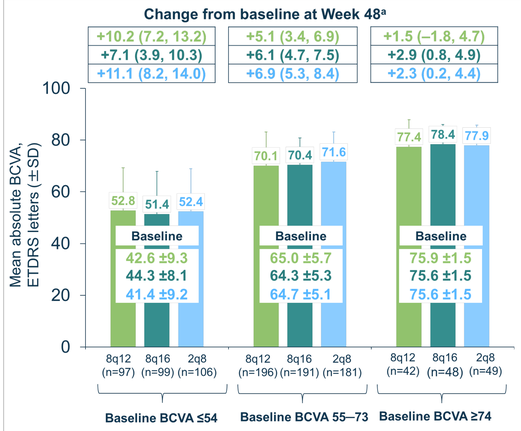
Stippled boxes = initial treatment phase; X = active injection; o = sham injections.

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

DRM 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

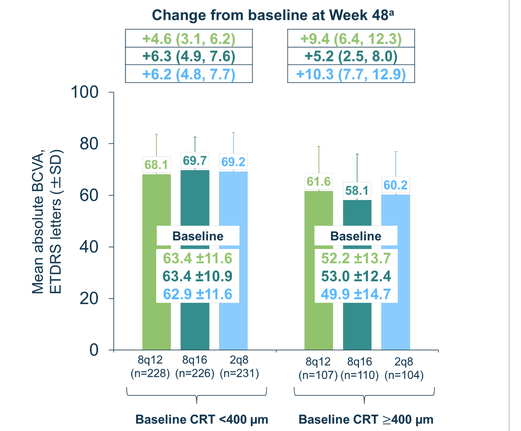
[a]At Week 36, patients on 8q16 who were previously shortened to q12 could have been shortened to q8. **BCVA**, best corrected visual acuity; **CRT,** central retinal thickness; **DRM**, dose regimen modification; **nAMD,** neovascular age-related macular degeneration; **Wk**, week.

FIGURE 2: BCVA by baseline BCVA categories (ETDRS letters): at Week 48



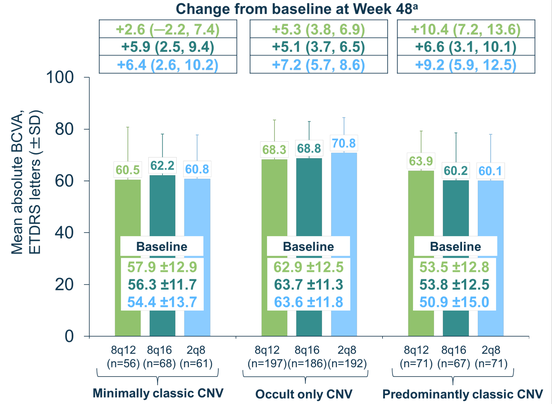
Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding. [a]Mean (95% CI) change from baseline to Week 48. **BCVA**, best corrected visual acuity; **ETDRS**, Early Treatment Diabetic Retinopathy Study.

FIGURE 3: BCVA by baseline CRT categories (µm): at Week 48



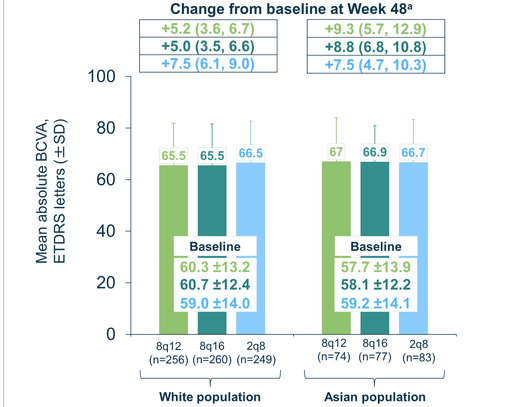
Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding. [a]Mean (95% CI) change from baseline to Week 48. **BCVA**, best corrected visual acuity; **CRT**, central retinal thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Study.

FIGURE 4: BCVA by baseline CNV type: at Week 48



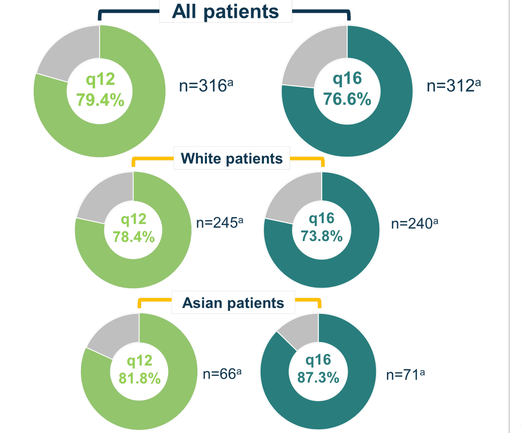
Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding. [a]Mean (95% CI) change from baseline to Week 48. **BCVA**, best corrected visual acuity; **CNV**, choroidal neovascularization; **ETDRS**, Early Treatment Diabetic Retinopathy Study.

FIGURE 5: BCVA by race: at Week 48



Error bars denote SD. Some baseline BCVA plus mean change at Week 48 BCVA values do not add up exactly to the Week 48 absolute BCVA values due to rounding. Data are not reported for Black or African American patients due to small sample size (n=2). [a]Mean (95% CI) change from baseline to Week 48. **BCVA**, best corrected visual acuity; **ETDRS**, Early Treatment Diabetic Retinopathy Study.

FIGURE 6: Proportion of patients maintaining 8 mg q12 and q16 dosing intervals up to Week 48: categorized by race



Data are not reported for Black or African American patients due to small sample size (n=2). [a]Patients completing Week 48.

CONCLUSIONS

In patients with nAMD, mean change in BCVA at Week 48 differed by baseline BCVA categories, as higher baseline BCVA is generally associated with smaller gains following treatment[1]. BCVA outcomes were comparable for 8 mg vs 2 mg among the evaluable subgroups of baseline characteristics.

The majority of White and Asian patients with nAMD treated with intravitreal aflibercept 8 mg maintained q12 or q16 week treatment intervals (Black or African American patients were excluded due to small sample size). These proportions are comparable to those for the overall patient populations in the PULSAR study.

References

1. Busch et al. *Acta Diabetol* 2019 56: 777-84

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

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