Additional Visual and Anatomic Outcomes of Intravitreal Aflibercept Injection 8 mg Versus 2 mg: A Post Hoc Analysis of the Phase 2 CANDELA Study

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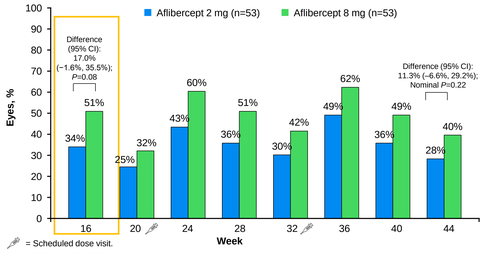
BACKGROUND & PURPOSE

- Aflibercept 8 mg has the potential to improve anatomic and functional outcomes in patients with neovascular age-related macular degeneration (nAMD) and is being investigated at dosing intervals of ≥12 weeks
- The Phase 2 proof-of-concept CANDELA study (NCT04126317) evaluated the safety as well as the visual and anatomic outcomes of aflibercept 8 mg versus aflibercept 2 mg[1]
  - The safety profile of aflibercept 8 mg was similar to aflibercept 2 mg with no new safety signals
  - At Week 16, 51% of eyes treated with aflibercept 8 mg were without retinal fluid in the center subfield compared with 34% of eyes with aflibercept 2 mg (**Figure 1**)
  - Additionally, change from baseline in best-corrected visual acuity (BCVA) and central subfield thickness (CST) outcomes favored aflibercept 8 mg
- In this post hoc analysis, the effect of aflibercept 8 mg on visual and anatomic outcomes in patients with nAMD was further examined

METHODS

- Treatment-naive adults (≥50 years) with active subfoveal choroidal neovascularization (CNV) secondary to nAMD and a BCVA of 78 to 24 letters (Snellen equivalent of 20/32 to 20/320) in the study eye were enrolled
- A total of 106 patients were randomized 1:1 to receive 3 monthly doses of either aflibercept 8 mg (n=53) or aflibercept 2 mg (n=53) followed by doses at Week 20 and 32 (**Figure 2**)
- Pro re nata (PRN) dosing was permitted at Weeks 24, 28, 36, or 40, if patients lost ≥5 letters from Week 20 due to disease progression or anatomic findings that were considered vision threatening (e.g., worsening/persistent retinal fluid, new/worsening retinal pigment epithelial detachment, new/persistent hemorrhage)
- Injection intervals >12 weeks were not investigated
- Outcomes assessed included:
  - The proportion of eyes without IRF, SRF, or subretinal pigment epithelium (sub-RPE) fluid in the center subfield was assessed at Weeks 16 and 44
  - Proportion of eyes with CST change at Week 44 by quartiles and the baseline characteristics of patients in the highest quartile (CST >239 µm)
  - Proportion of eyes that with BCVA changes and the baseline characteristics of those achieving ≥15-letter gain
  - Proportion of eyes that achieved BCVA of ≥20/40 and ≥20/20 at Week 44
  - Proportion of eyes with baseline BCVA <20/40 that achieved ≥10- and ≥15-letter gains at Week 44

Figure 1. Primary Efficacy Endpoint: Proportion of Eyes Without Retinal Fluid in the Center Subfield



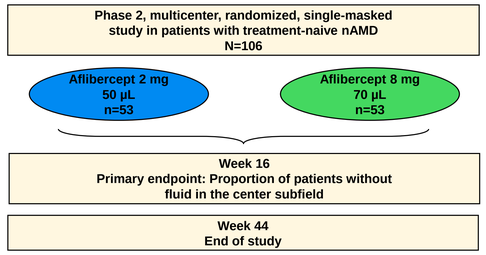
= Scheduled dose visit.

Mean number of injections	Aflibercept 2 mg	Aflibercept 8 mg
	5.8	5.8

Without fluid defined as **no** IRF and **no** SRF. Full analysis set, last observation carried forward (LOCF).
For patients receiving additional treatment at Week 16, measurements past Week 16 were imputed using the LOCF prior to additional treatment. CI, confidence interval.

Figure 2. (A) Study Design and (B) Dosing Schedule

(A)



(B)

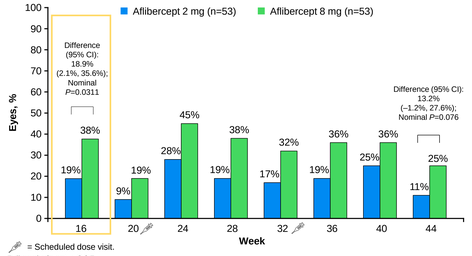
	Screen 1 and 2	Day 1 (BL)	Week 4	8	12	16	20	24	28	32	36	40	44[a]
Aflibercept 2 mg		X	X	X			X	PRN	PRN	X	PRN	PRN	
Aflibercept 8 mg		X	X	X			X	PRN	PRN	X	PRN	PRN	

Additional treatment allowed based on investigator assessment after discussion with sponsor; data censored after rescue

[a]End of study.
BL, baseline.

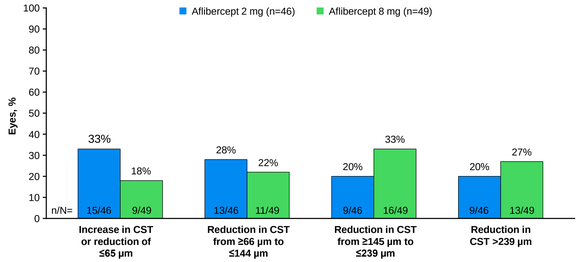
RESULTS

Figure 3. Proportion of Eyes Without IRF, SRF, and Sub-RPE Fluid in the Center Subfield



= Scheduled dose visit.
Full analysis set, LOCF.
For patients receiving additional treatment at Week 16, measurements past Week 16 were imputed using the LOCF prior to additional treatment.

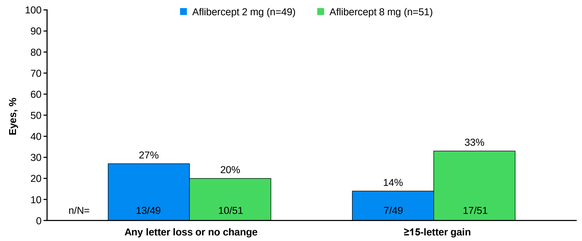
Figure 4. Proportion of Eyes With CST Change by Quartiles and Baseline Characteristics of Eyes With CST Reductions of >239 µm at Week 44



Baseline characteristics of eyes with CST reductions >239 µm	Aflibercept 2 mg	Aflibercept 8 mg
BCVA, letters		
Mean	47.1	47.5
Median	50.0	54.0
Range (min, max)	33, 59	23, 74
CST, µm		
Mean	788.2	702.2
Median	650.0	688.0
Range (min, max)	485, 1271	510, 990

Full analysis set, patients who had evaluable CST at Week 44 visit.
All observed values used for analysis.

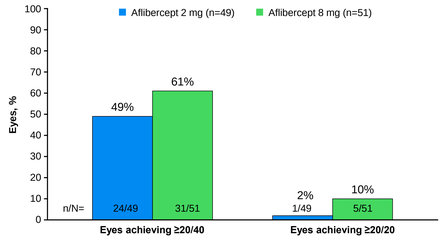
Figure 5. Proportion of Eyes with BCVA Changes and Baseline Characteristics of Eyes With ≥15-Letter Gains at Week 44



Baseline characteristics of eyes with ≥15-letter gains at Week 44	Aflibercept 2 mg	Aflibercept 8 mg
BCVA, letters		
Mean	55.4	53.8
Median	56.0	56.0
Range (min, max)	43, 63	23, 72
CST, µm		
Mean	579.0	554.9
Median	567.0	557.0
Range (min, max)	360, 819	371, 990

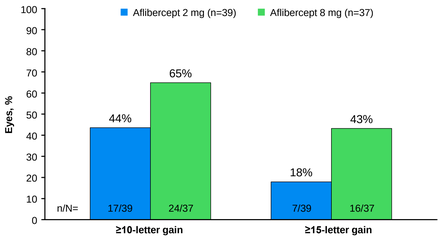
Full analysis set, patients who completed Week 44 visit.
All observed values used for analysis.

Figure 6. Proportion of Eyes That Achieved BCVA of ≥20/40 and ≥20/20 at Week 44



Full analysis, patients who completed Week 44 visit.
20/40 was defined as ≥69 ETDRS letters; 20/20 was defined as ≥84 ETDRS letters. All observed values used for analysis.
ETDRS, Early Treatment Diabetic Retinopathy Study.

Figure 7. Proportion of Eyes With Baseline BCVA <20/40 With ≥10- and ≥15-Letter Gains at Week 44



Full analysis set, patients who completed Week 44 visit and with BCVA <20/40 (69 ETDRS letters) at baseline.
All observed values used for analysis.

CONCLUSIONS

- A higher proportion of eyes treated with aflibercept 8 mg versus aflibercept 2 mg had no IRF, SRF, or sub-RPE fluid in the center subfield at every visit starting at Week 16
- More eyes treated with aflibercept 8 mg were in the quartiles of greater BCVA and CST improvement from baseline to Week 44; these benefits were not driven by baseline imbalances
- More eyes treated with aflibercept 8 mg achieved clinically meaningful BCVA threshold of ≥20/40 and ≥20/20 at Week 44

REFERENCE

1. Brown DM et al. Angiogenesis 2022, Virtual.

ACKNOWLEDGMENTS & DISCLOSURES

- Jordana G Fein has served as a consultant for Regeneron Pharmaceuticals, Inc., Bausch and Lomb, Genentech/Roche, and Apellis; and has served on a speaker's bureau for Regeneron Pharmaceuticals, Inc., Genentech/Roche, and Apellis Pharmaceuticals
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