A 96-week PULSAR subgroup analysis: Similar visual and anatomic improvements with aflibercept 8 mg every 12 weeks or longer and 2 mg every 8 weeks, as defined by baseline BCVA, CRT, CNV type, and race

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PULSAR: Multicenter, randomized, double-masked study

pulsar nAMD

Patients with treatment-naïve nAMD, randomized at baseline

2q8
Aflibercept 2 mg every 8 weeks after 3 initial monthly injections
n=336

8q12
Aflibercept 8 mg every 12 weeks after 3 initial monthly injections
n=335

8q16
Aflibercept 8 mg every 16 weeks after 3 initial monthly injections
n=338

	YEAR 1													YEAR 2											
	Day 1	W4	W8	W12	W16	W20	W24	W28	W32	W36	W40	W44	W48	W52	W56	W60	W64	W68	W72	W76	W80	W84	W88	W92	W96
2q8	X	X	X		X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	X	o	–
8q12	X	X	X		o[a]	X[a]	o	o	X[a]	o	o	X[a]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	o	o	X[a,b]	–
8q16	X	X	X		o[a]	o[a]	X[a]	o	o	o	X[a]	o	o	o	X[a,b]	o	o	o	X[a,b]	o	o	o	X[a,b]	o	–

Primary endpoint at W48:
Mean change in BCVA (non-inferiority)

End of study at W96
with optional ~1-year extension through W156

[a]DRM: Interval Shortening During Years 1 and 2

Criteria for interval shortening
- >5-letter loss in BCVA compared with Week 12 due to persistent or worsening nAMD **AND**
- >25 µm increase in CRT compared with Week 12, **OR** new foveal neovascularization, **OR** new foveal hemorrhage

- Patients who met DRM criteria had dosing intervals shortened to q8 at **Weeks 16** and **20** or by 4-week increments from **Week 24**
  - The minimum assigned dosing interval was q8

[b]DRM: Interval Extension During Year 2

Criteria for interval extension
- <5-letter loss in BCVA compared with Week 12 **AND**
- No fluid at the central subfield on OCT **AND**
- No new foveal hemorrhage or foveal neovascularization

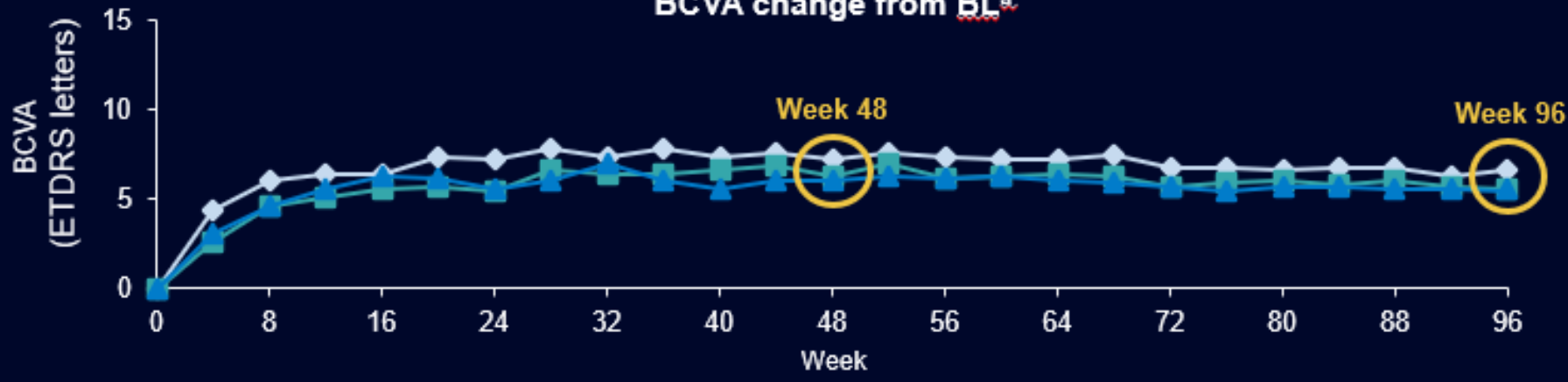
- Patients who met DRM criteria from **Weeks 52 through 96** had dosing intervals extended by 4-week increments
  - The maximum assigned dosing interval was q24

Figure does not reflect all dosing options once a patient's dosing interval is shortened or extended. Stippled boxes = initial treatment phase; X = active injection; o = sham injections.
q8, every 8 weeks; **q24**, every 24 weeks; **BCVA**, best-corrected visual acuity; **CRT**, central retinal thickness; **DRM**, dose regimen modification; **nAMD**, neovascular age-related macular degeneration; **OCT**, optical coherence tomography; **W**, week.

BCVA and CRT through Week 96: Comparable outcomes with aflibercept 8 mg and 2 mg overall

pulsar nAMD

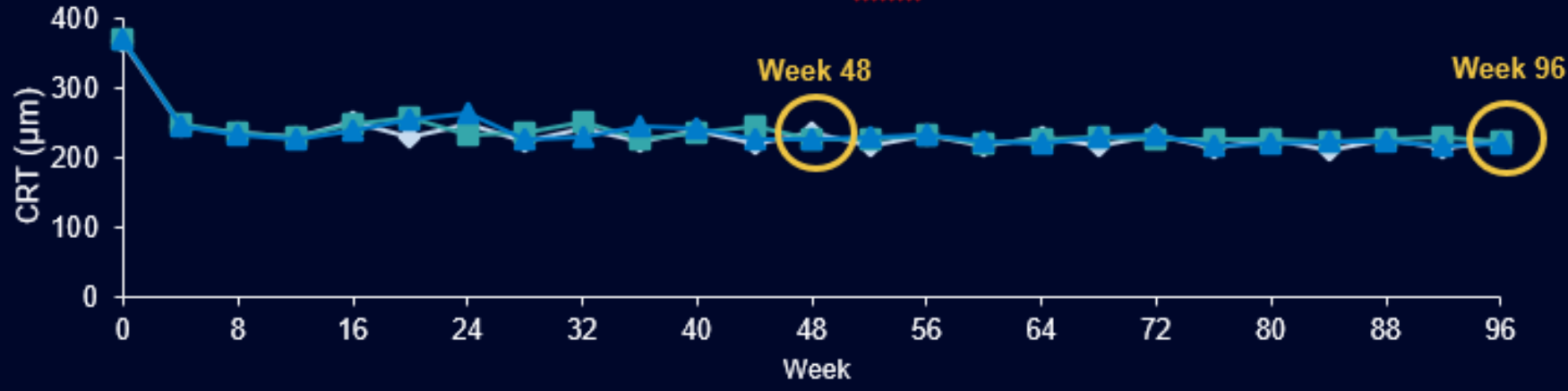
BCVA change from BL[a]



LS means[a,b]

	Week 48	Week 96
2q8	+7.0	+6.6
8q12	+6.1	+5.6
8q16	+5.9	+5.5

Absolute CRT[c]



LS means[a,b]

	Week 48	Week 96
2q8	−136	−147
8q12	−147	−152
8q16	−147	−149

FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338 (at BL). [a]LS mean values (data post-ICE were censored); [b]LS means were generated using MMRM, with baseline BCVA measurement (for BCVA analysis) or BL CRT measurement (for CRT analysis) as a covariate, and treatment group (aflibercept 2q8, 8q12, 8q16), visit, and stratification variables (geographic region [Japan vs. Rest of World] and BL BCVA [<60 vs. ≥60]) as fixed factors, and interaction terms for BL and visit and for treatment and visit. [c]Observed values.

BL, baseline; **FAS**, full analysis set, **ICE**, intercurrent event; **LS**, least squares; **MMRM**, mixed model for repeated measures.

Baseline characteristics

pulsar nAMD

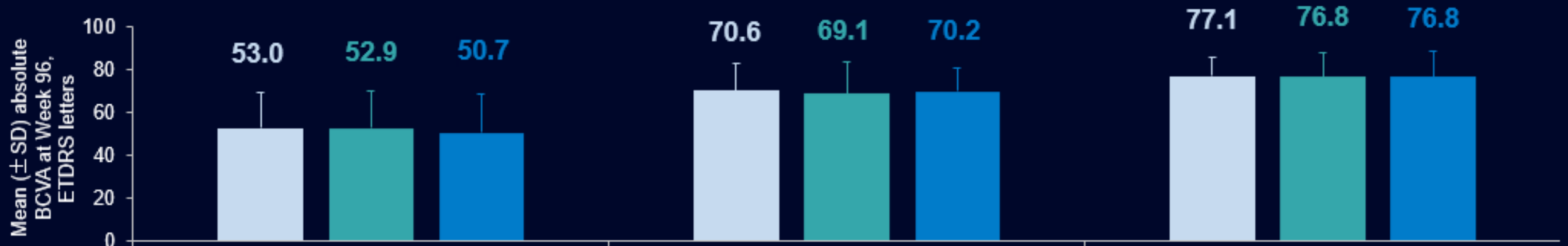
	2q8	8q12	8q16	All 8mg	Total
Randomized, n	336	335	338	673	1009
Age, years	74.2 (8.8)	74.7 (7.9)	74.5 (8.5)	74.6 (8.2)	74.5 (8.4)
Female, %	56.0	54.3	53.3	53.8	54.5
Race, %					
Asian	24.7	22.1	22.8	22.4	23.2
Black or African American	0.6	0.6	0	0.3	0.4
White	74.1	76.4	76.9	76.7	75.8
Not reported	0.6	0.6	0.3	0.4	0.5
BCVA, ETDRS letters	58.9 (14.0)	59.9 (13.4)	60.0 (12.4)	59.9 (12.9)	59.6 (13.3)
CRT, µm	367 (134)	370 (124)	371 (133)	371 (128)	370 (130)
CNV size, mm^2	6.4 (5.0)	6.0 (4.8)	6.5 (5.5)	6.3 (5.2)	6.3 (5.1)
CNV type, %					
Minimally classic CNV	18.2	16.7	20.1	18.4	18.3
Occult-only CNV	57.1	58.8	55.0	56.9	57.0
Predominantly classic CNV	21.1	21.2	19.8	20.5	20.7

FAS. Data are mean (SD) unless otherwise indicated.
CNV, choroidal neovascularization; **ETDRS**, Early Treatment of Diabetic Retinopathy Study; **SD**, standard deviation.

BCVA outcomes with aflibercept 8 mg and 2 mg at Week 96 are independent of BL BCVA

pulsar nAMD

Mean (95% CI) BCVA (ETDRS letters) change from BL at Week 96	BL BCVA ≤54	BL BCVA 55–73	BL BCVA ≥74
2q8	+11.7 (8.8, 14.7)	+5.9 (4.2, 7.6)	+1.5 (−0.8, 3.9)
8q12	+10.4 (7.0, 13.7)	+4.1 (2.1, 6.1)	+0.9 (−2.6, 4.3)
8q16	+6.5 (2.9, 10.0)	+5.9 (4.4, 7.5)	+1.1 (−2.1, 4.4)



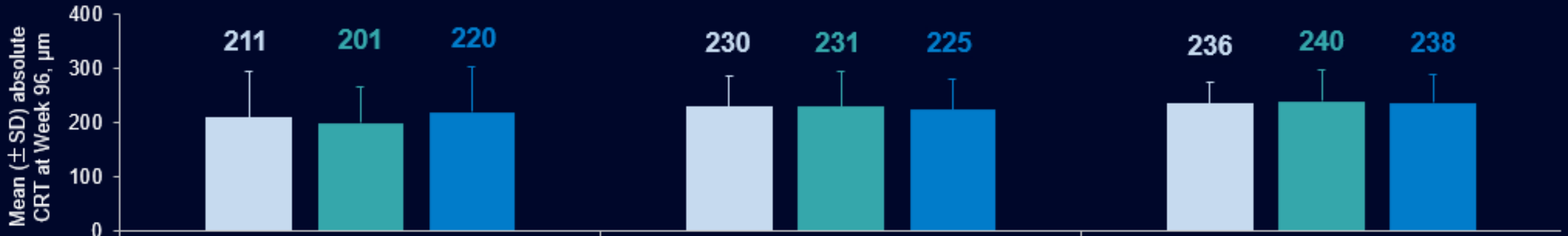
	2q8 (n=106)	8q12 (n=97)	8q16 (n=99)	2q8 (n=181)	8q12 (n=196)	8q16 (n=191)	2q8 (n=49)	8q12 (n=42)	8q16 (n=48)
BL	41.4	42.6	44.3	64.7	65.0	64.3	75.6	75.9	75.6
Week 48	52.4	52.8	51.4	71.6	70.1	70.3	77.9	77.4	78.4

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL BCVA.
CI, confidence interval; LOCF, last observation carried forward.

CRT improvements with aflibercept 8 mg and 2 mg at Week 96 are independent of BL BCVA

pulsar nAMD

Mean CRT (µm) change (95% CI) from BL at Week 96	BL BCVA ≤54	BL BCVA 55–73	BL BCVA ≥74
2q8	−224 (−255, −193)	−115 (−129, −100)	−58 (−75, −42)
8q12	−254 (−283, −224)	−109 (−121, −96)	−76 (−101, −51)
8q16	−237 (−270, −205)	−112 (−126, −97)	−82 (−107, −58)



	2q8 (n=106)	8q12 (n=97)	8q16 (n=99)	2q8 (n=181)	8q12 (n=196)	8q16 (n=190)	2q8 (n=48)	8q12 (n=42)	8q16 (n=47)
BL	439	454	457	344	339	338	294	322	322
Week 48	227	217	226	239	232	225	243	236	237

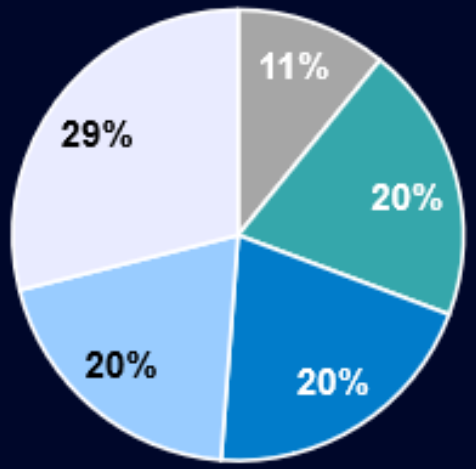
FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL CRT.

Last assigned treatment intervals at Week 96 categorized by BL BCVA

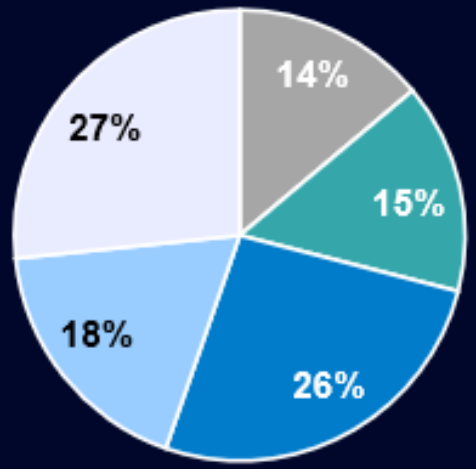
pulsar nAMD

BL BCVA categories

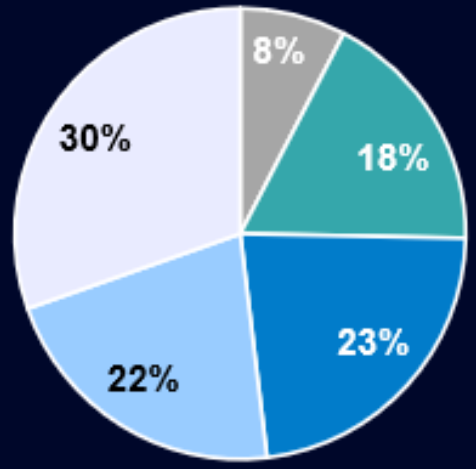
≤54 ETDRS letters (n=166)



55–73 ETDRS letters (n=338)



≥74 ETDRS letters (n=79)



All patients receiving aflibercept 8 mg

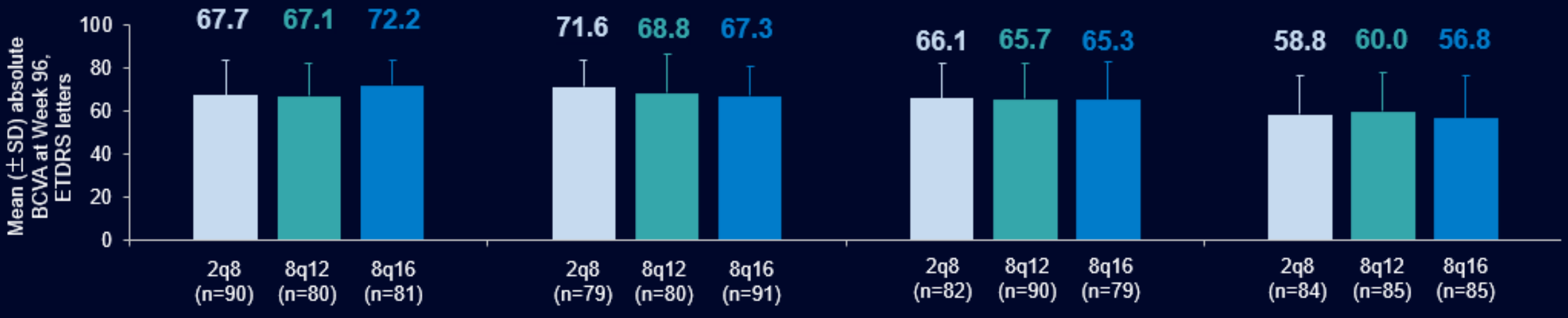
Last assigned treatment interval: q8 q12 q16 q20 q24[a]

Data shown for patients who completed 96 weeks of treatment.
Values may not add up to 100% due to rounding.
[a]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

BCVA outcomes with aflibercept 8 mg and 2 mg at Week 96 are independent of BL CRT

pulsar nAMD

Mean (95% CI) BCVA (ETDRS letters) change from BL at Week 96	≤278 µm	279–343 µm	344–422 µm	≥423 µm
2q8	+4.8 (2.2, 7.4)	+6.3 (3.8, 8.8)	+6.9 (4.1, 9.7)	+10.4 (7.2, 13.6)
8q12	+3.1 (0.7, 5.4)	+4.2 (0.3, 8.0)	+5.2 (2.4, 8.1)	+9.3 (5.7, 12.9)
8q16	+7.4 (5.3, 9.5)	+5.0 (2.6, 7.4)	+4.3 (0.9, 7.7)	+4.8 (1.2, 8.3)



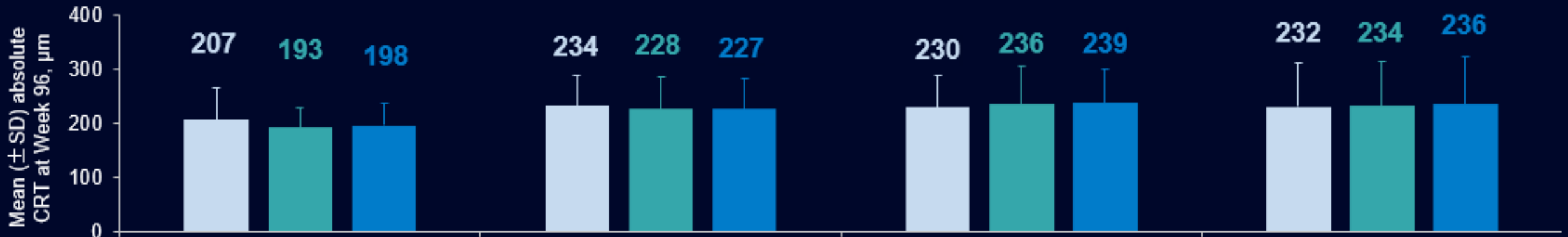
	2q8 (n=90)	8q12 (n=80)	8q16 (n=81)	2q8 (n=79)	8q12 (n=80)	8q16 (n=91)	2q8 (n=82)	8q12 (n=90)	8q16 (n=79)	2q8 (n=84)	8q12 (n=85)	8q16 (n=85)
BL	62.8	64.1	64.8	65.2	64.6	62.3	59.2	60.5	60.9	48.4	50.7	52.0
Week 48	67.7	68.3	72.3	71.5	69.3	68.0	67.6	65.9	67.1	59.1	60.9	56.4

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL BCVA.

CRT improvements with aflibercept 8 mg and 2 mg at Week 96 are independent of BL CRT

pulsar nAMD

Mean (95% CI) CRT (µm) change from BL at Week 96	≤278 µm	279–343 µm	344–422 µm	≥423 µm
2q8	−32 (−45, −19)	−79 (−91, −66)	−146 (−161, −132)	−310 (−335, −285)
8q12	−49 (−58, −40)	−80 (−94, −67)	−143 (−157, −128)	−308 (−335, −280)
8q16	−41 (−50, −33)	−82 (−94, −69)	−142 (−156, −128)	−317 (−347, −288)

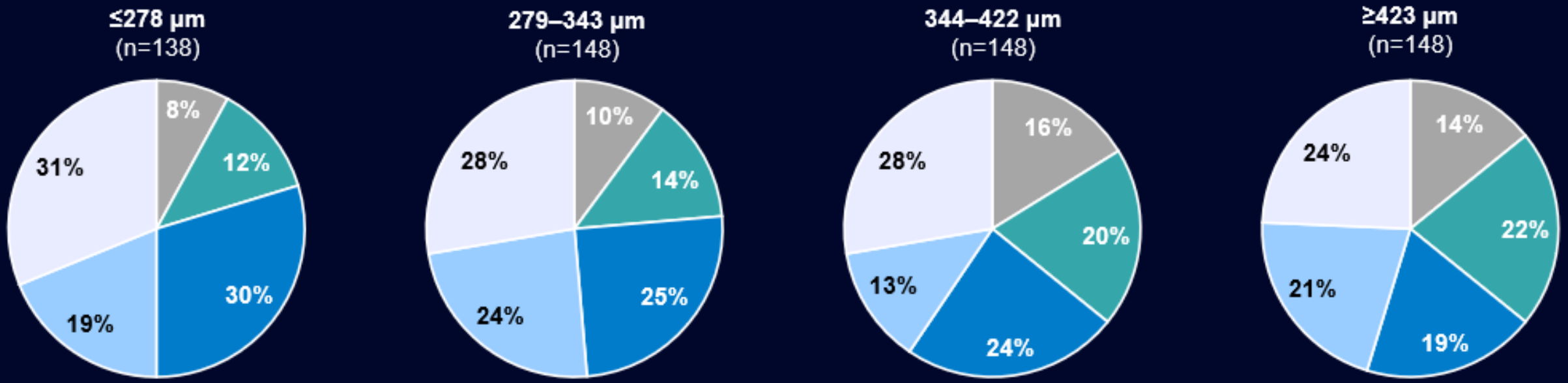


	2q8	8q12	8q16	2q8	8q12	8q16	2q8	8q12	8q16	2q8	8q12	8q16
BL	239	242	239	312	309	309	376	379	381	547	541	553
Week 48	210	194	198	246	231	225	240	238	238	250	249	247

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL CRT.

Last assigned treatment intervals at Week 96 categorized by BL CRT

pulsar nAMD

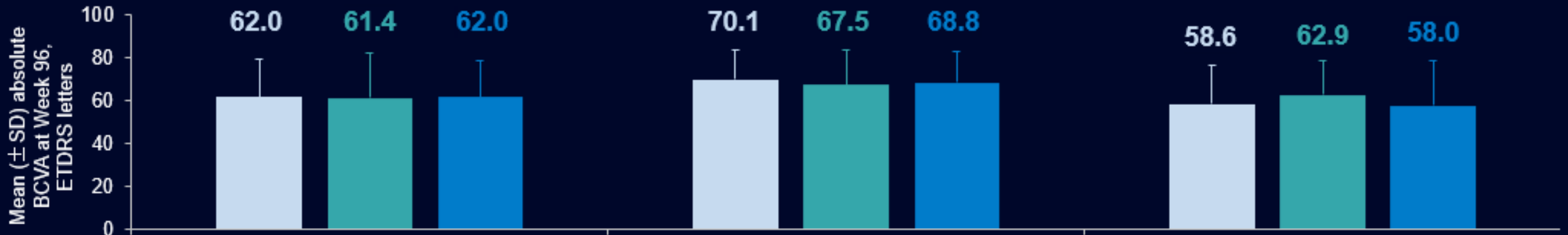


Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding.
[a]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

BCVA outcomes with aflibercept 8 mg and 2 mg at Week 96 are independent of BL CNV type

pulsar nAMD

Mean (95% CI) BCVA (ETDRS letters) change from BL at Week 96	Minimally classic	Occult only	Predominantly classic
2q8	+7.4 (3.2, 11.6)	+6.6 (5.1, 8.1)	+7.7 (4.1, 11.3)
8q12	+3.5 (−1.5, 8.5)	+4.4 (2.5, 6.2)	+9.4 (6.0, 12.8)
8q16	+5.8 (2.0, 9.6)	+5.2 (3.6, 6.8)	+4.3 (0.2, 8.5)



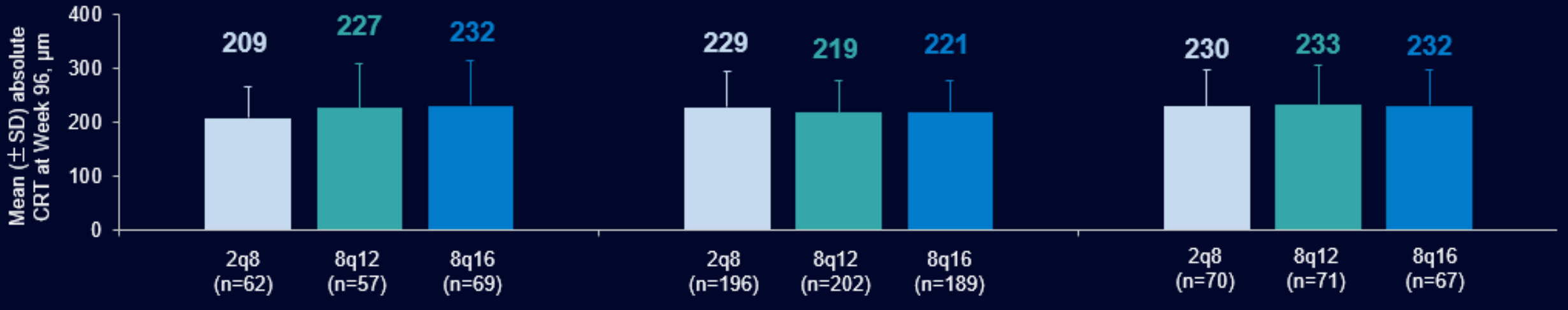
BL	54.5	57.9	56.2	63.4	63.1	63.5	50.9	53.5	53.8
Week 48	61.0	60.6	62.5	70.6	68.4	68.8	60.1	63.9	60.2

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL BCVA.

CRT improvements with aflibercept 8 mg and 2 mg at Week 96 are independent of BL CNV type

pulsar nAMD

Mean CRT (µm) change (95% CI) from BL at Week 96	Minimally classic	Occult only	Predominantly classic
2q8	−190 (−222, −157)	−98 (−114, −83)	−204 (−240, −169)
8q12	−171 (−206, −135)	−118 (−133, −103)	−196 (−231, −161)
8q16	−179 (−210, −149)	−116 (−133, −98)	−190 (−229, −150)

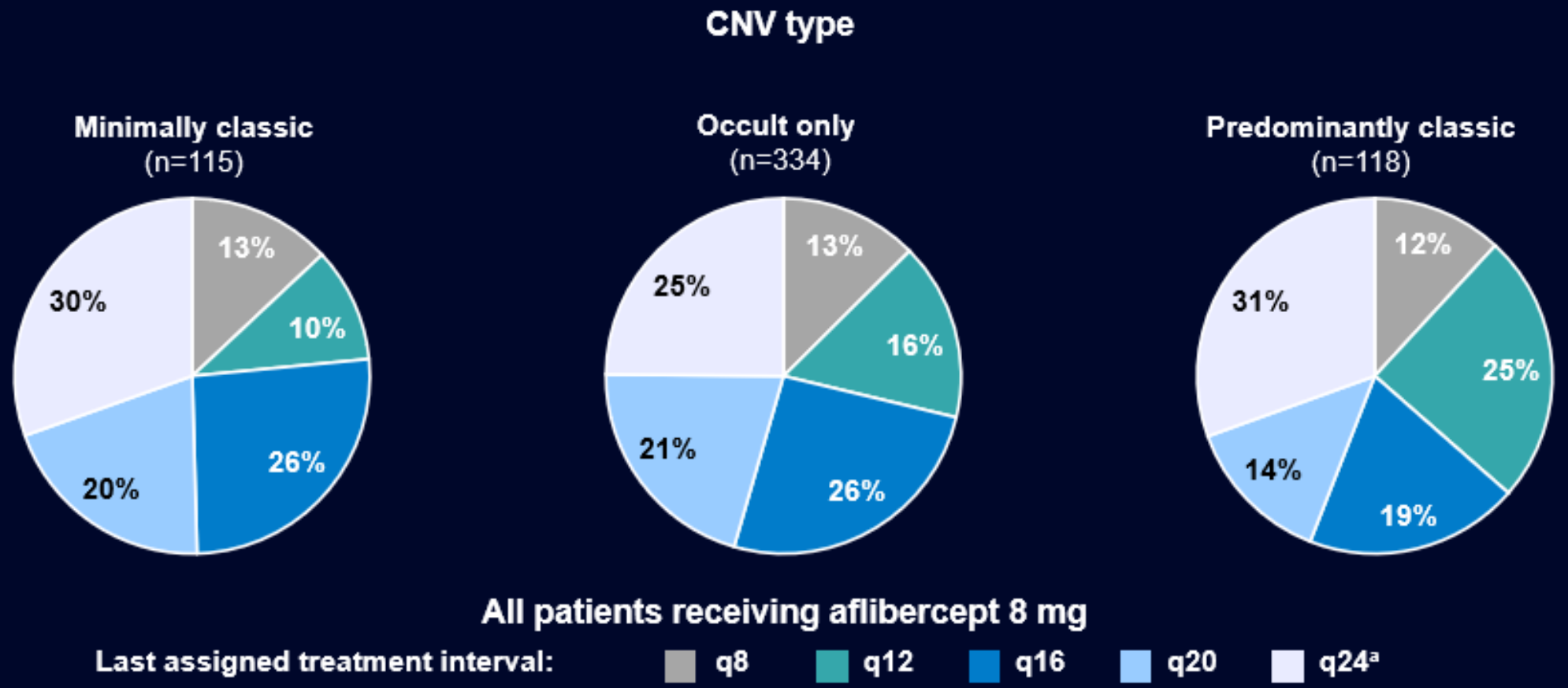


	2q8 (n=62)	8q12 (n=57)	8q16 (n=69)	2q8 (n=196)	8q12 (n=202)	8q16 (n=189)	2q8 (n=70)	8q12 (n=71)	8q16 (n=67)
BL	411	399	411	326	338	337	434	428	423
Week 48	219	231	231	235	220	224	252	250	237

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL CRT.

Last assigned treatment intervals at Week 96 categorized by BL CNV type

pulsar nAMD

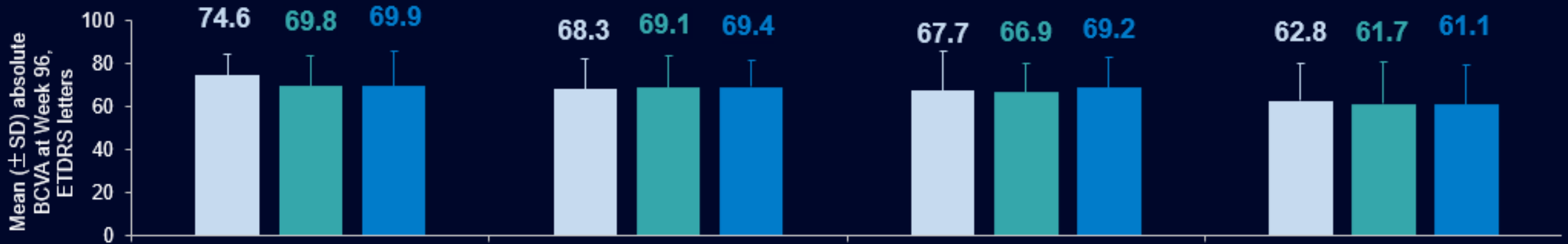


Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding.
[a]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

BCVA outcomes with aflibercept 8 mg and 2 mg at Week 96 are independent of baseline CNV size

pulsar nAMD

Mean (95% CI) BCVA (ETDRS letters) change from BL at Week 96	<1.3 mm²	1.3–<4 mm²	4–<5 mm²	≥5 mm²
2q8	+10.7 (6.3, 15.2)	+8.2 (5.8, 10.6)	+5.5 (1.2, 9.8)	+6.0 (3.9, 8.1)
8q12	+7.0 (2.8, 11.2)	+7.9 (5.1, 10.7)	+5.5 (1.1, 9.8)	+3.7 (1.2, 6.3)
8q16	+7.8 (3.9, 11.7)	+8.2 (5.9, 10.5)	+4.2 (1.1, 7.3)	+3.5 (1.2, 5.8)



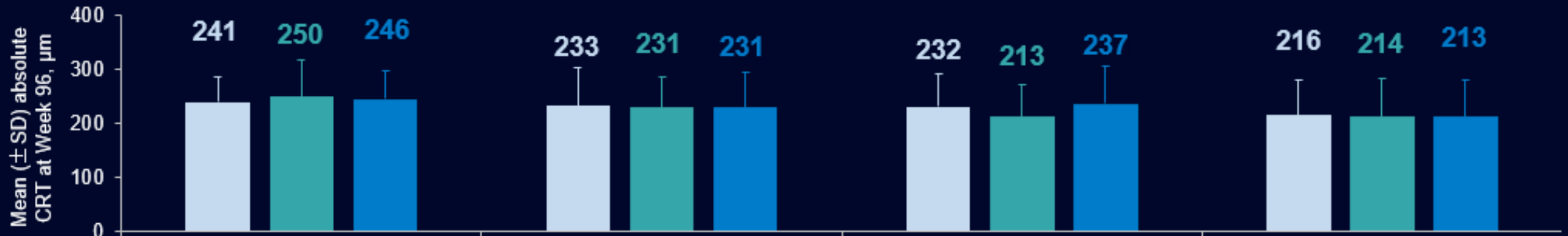
	2q8	8q12	8q16	2q8	8q12	8q16	2q8	8q12	8q16	2q8	8q12	8q16
BL	63.9	62.8	62.0	60.0	61.1	61.2	62.2	61.4	65.1	56.8	58.0	57.6
Week 48	75.3	70.5	71.5	68.7	70.0	68.5	69.6	66.6	71.1	62.9	62.5	61.6

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL BCVA.

CRT improvements with aflibercept 8 mg and 2 mg at Week 96 are independent of BL CNV size

pulsar nAMD

Mean (95% CI) CRT (µm) change from BL at Week 96	<1.3 mm²	1.3–<4 mm²	4–<5 mm²	≥5 mm²
2q8	−119 (−158, −80)	−138 (−164, −111)	−157 (−205, −109)	−144 (−164, −123)
8q12	−102 (−133, −71)	−155 (−184, −126)	−135 (−173, −97)	−157 (−177, −137)
8q16	−126 (−165, −86)	−135 (−164, −106)	−109 (−144, −75)	−165 (−186, −144)



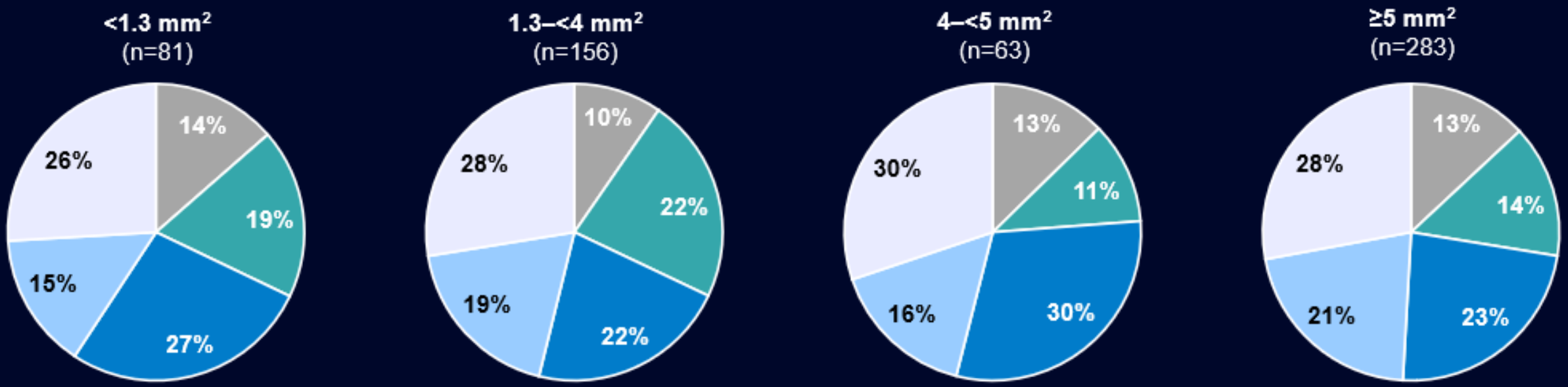
	2q8	8q12	8q16	2q8	8q12	8q16	2q8	8q12	8q16	2q8	8q12	8q16
BL	360	352	372	368	384	367	389	348	346	364	372	378
Week 48	244	256	241	242	237	233	240	213	237	229	219	218

FAS, LOCF. N values for BL. Analyses were not adjusted for multiplicity or to allow for differences in BL CRT.

Last assigned treatment intervals at Week 96 categorized by BL CNV size

pulsar nAMD

Baseline CNV size



All patients receiving aflibercept 8 mg

Last assigned treatment interval: q8 q12 q16 q20 q24[a]

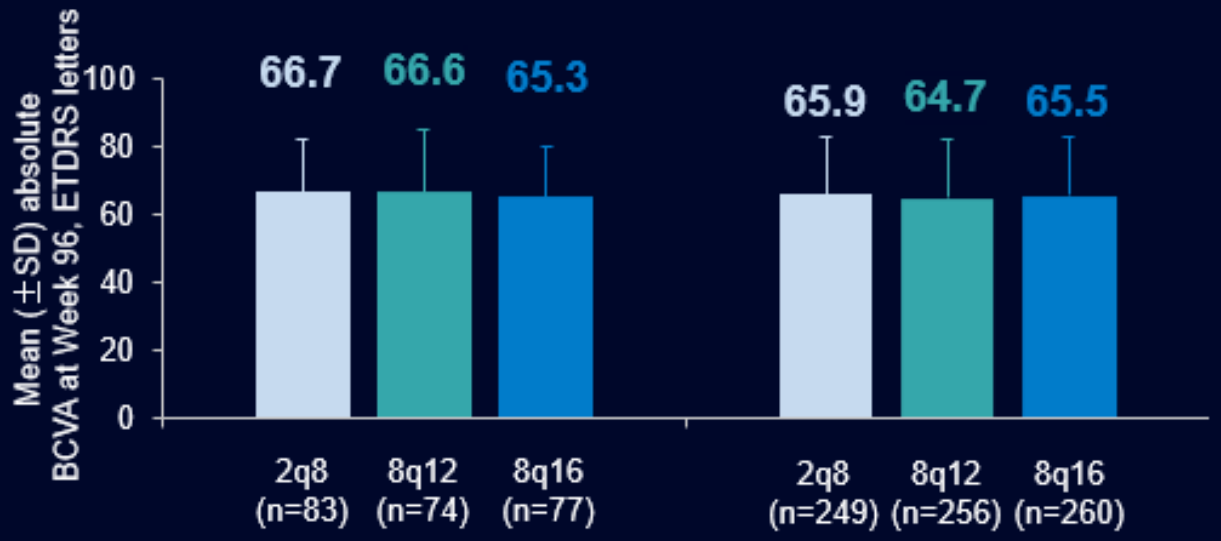
Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding.
[a]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

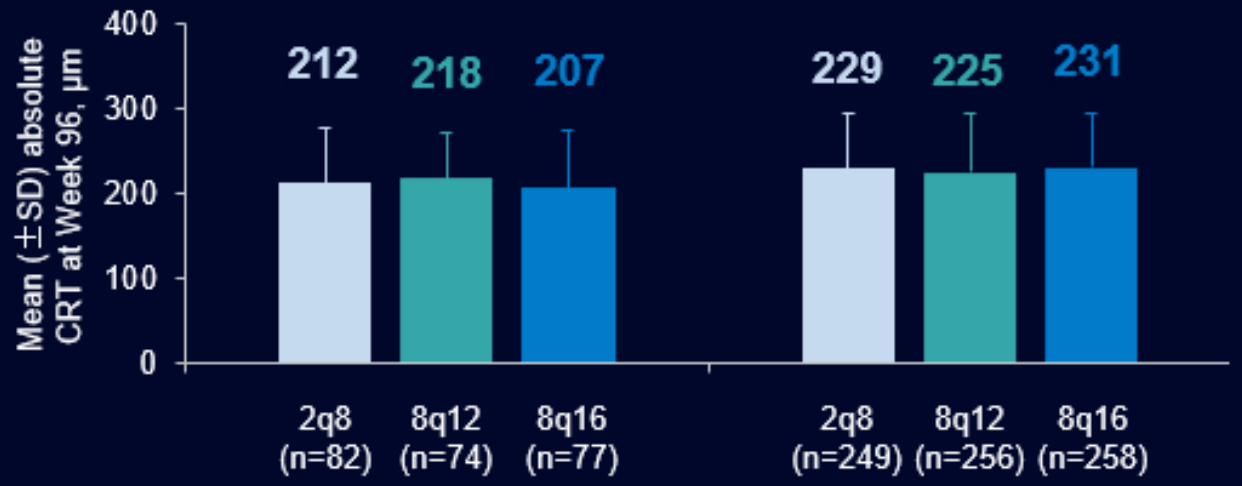
Visual and anatomic outcomes with aflibercept 8 mg and 2 mg at Week 96 are independent of race

pulsar nAMD

Mean (95% CI) BCVA (ETDRS letters) and CRT (μm) change from BL at Week 96

	Asian	White	Asian	White
2q8	+7.5 (4.8, 10.3)	+6.9 (5.3, 8.6)	−144 (−176, −111)	−138 (−154, −123)
8q12	+8.9 (5.1, 12.8)	+4.4 (2.6, 6.1)	−147 (−179, −115)	−147 (−163, −132)
8q16	+7.2 (4.8, 9.6)	+4.8 (3.1, 6.5)	−140 (−169, −112)	−146 (−163, −129)



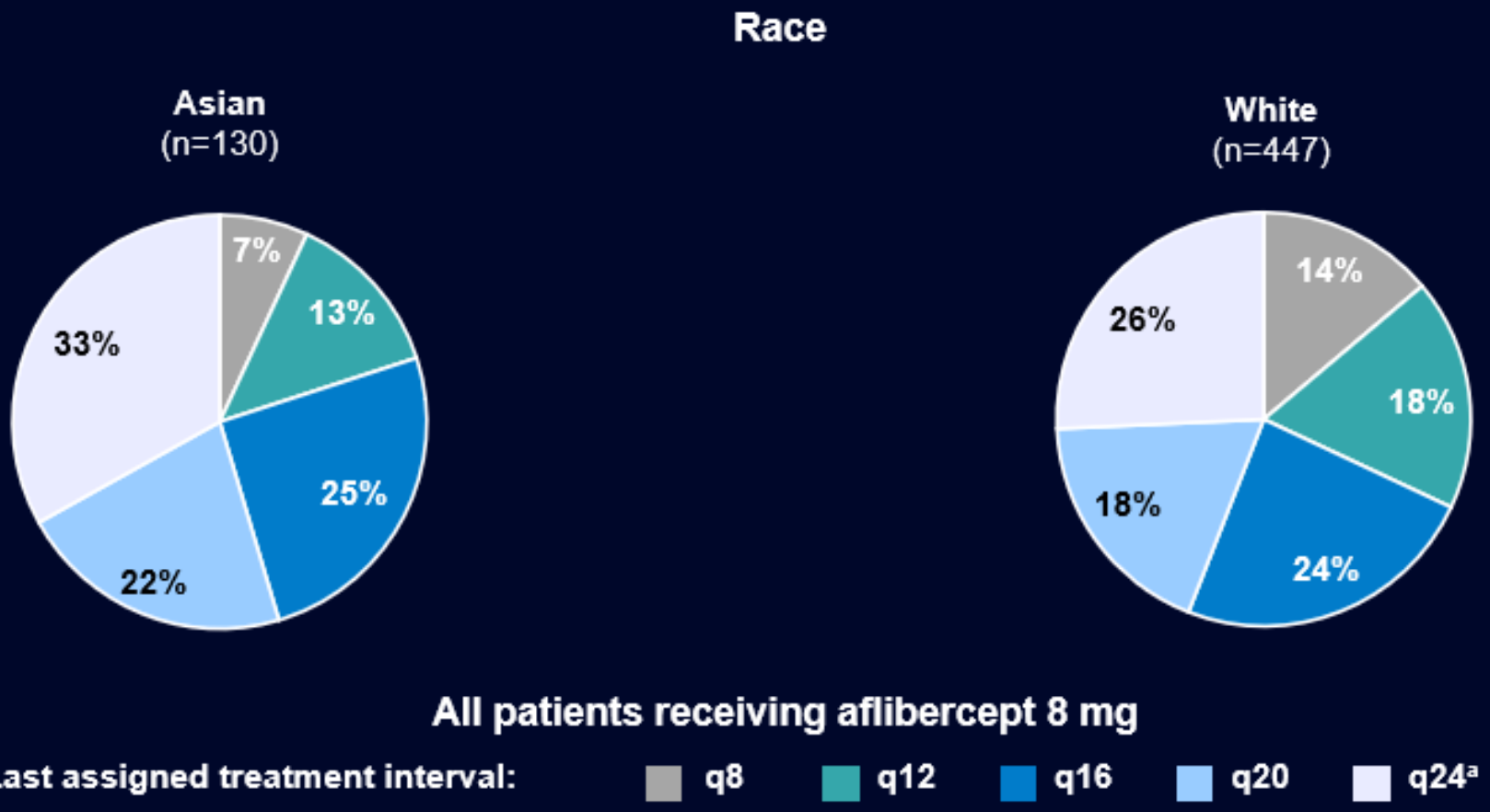


	BCVA			CRT		
	2q8	8q12	8q16	2q8	8q12	8q16
BL	59.2 (n=83)	57.7 (n=74)	58.1 (n=77)	59.0 (n=249)	60.3 (n=256)	60.7 (n=260)
Week 48	66.7 (n=83)	67.0 (n=74)	66.8 (n=77)	66.5 (n=249)	65.5 (n=256)	65.7 (n=260)
BL	365 (n=82)	366 (n=74)	347 (n=77)	366 (n=249)	373 (n=256)	377 (n=258)
Week 48	216 (n=82)	217 (n=74)	201 (n=77)	242 (n=249)	232 (n=256)	235 (n=258)

FAS, LOCF. Analyses were not adjusted for multiplicity or to allow for differences in BL BCVA or CRT. Data are not reported for Black or African American patients due to small sample size (n=2).

Last assigned treatment intervals at Week 96 categorized by race

pulsar nAMD



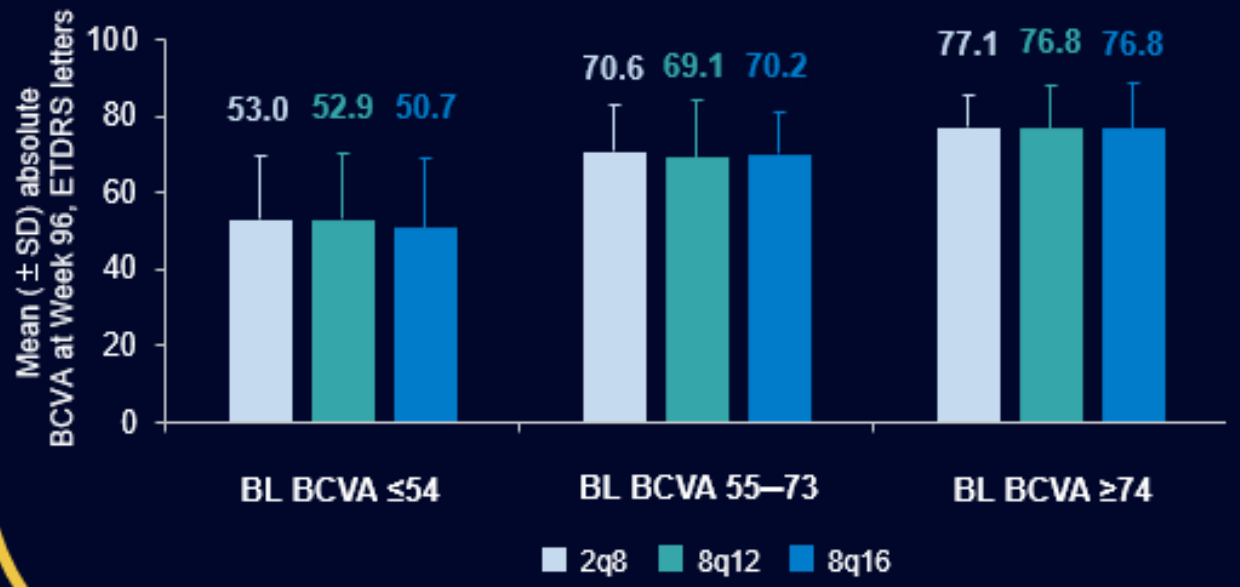
Data shown for patients who completed 96 weeks of treatment. Values may not add up to 100% due to rounding.
Data are not reported for Black or African American patients due to small sample size (n=2).
[a]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

Conclusions

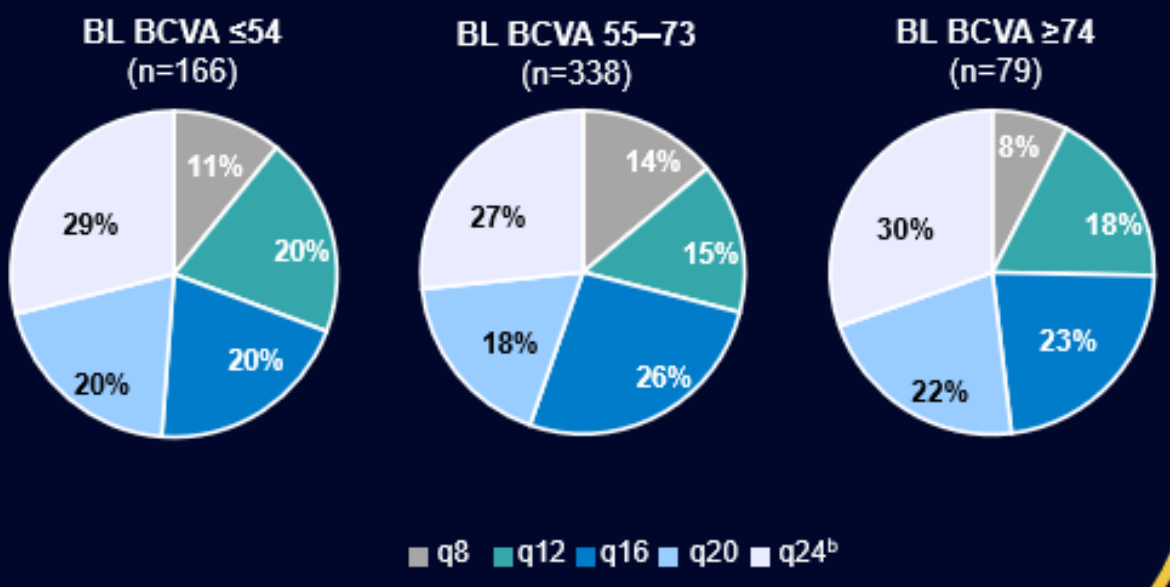
pulsar nAMD

- At Week 96, mean absolute and change in BCVA and CRT values were similar after treatment with aflibercept 8 mg with extended treatment intervals compared with 2 mg every 8 weeks **across all subgroups based on** baseline BCVA, CRT, CNV type and size, and race.
- Proportion of patients with maintained, extended, or shortened **treatment intervals** through Week 96 was **also independent of baseline characteristics**

Week 96 BCVA outcomes according to BL BCVA



Last assigned treatment interval according to BL BCVA[a]



[a]Values may not add up to 100% due to rounding. [b]Patients assigned to a 24-week dosing interval did not have enough time to complete the interval within the 96-week study period.

Thank you!

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