



A 96-Week PULSAR Phase 3 Trial *Post-hoc* Analysis: Rapid and Sustained Fluid Control with Aflibercept 8 mg Every 12 Weeks or Longer, as Defined by Fluid-Free Status at Weeks 16, 48, and 96 Stratified by Baseline CRT and BCVA

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Disclosures



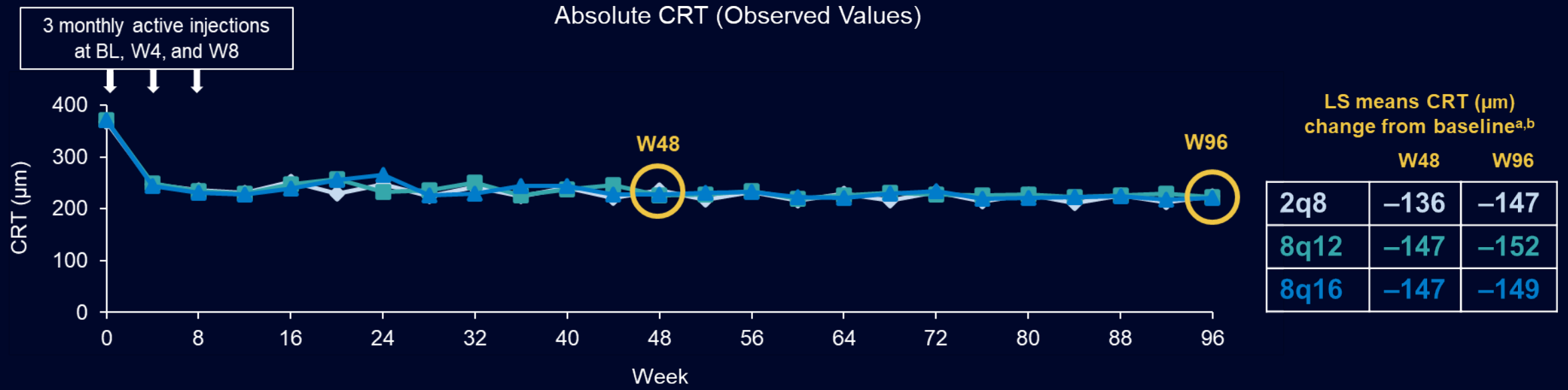
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PULSAR: 96-Week, Multicenter, Double-Masked Study in Patients with Treatment-Naïve nAMD



Patients were randomly assigned (1:1:1) to receive aflibercept 8q12 (n=335), 8q16 (n=338), or 2q8 (n=336), each after 3 monthly injections

At W48, aflibercept 8 mg demonstrated non-inferior BCVA gains with extended dosing intervals versus aflibercept 2 mg in patients with nAMD,¹ with no new safety signals



FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338 (at BL). ^aLS mean values (data post-ICE were censored); ^bLS means were generated using MRMM, with baseline CRT measurement 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 baseline and visit and for treatment and visit. **2q8**, aflibercept 2 mg every 8 weeks; **8q12**, aflibercept 8 mg every 12 weeks; **8q16**, aflibercept 8 mg every 16 weeks; **BCVA**, best-corrected visual acuity; **BL**, baseline; **CRT**, central subfield retinal thickness; **FAS**, full analysis set; **ICE**, intercurrent event; **LS**, least squares; **MRMM**, mixed model for repeated measures; **nAMD**, neovascular age-related macular degeneration; **W**, week. ¹Lanzetta P, et al. *Lancet*. 2024;403:1141–1152.

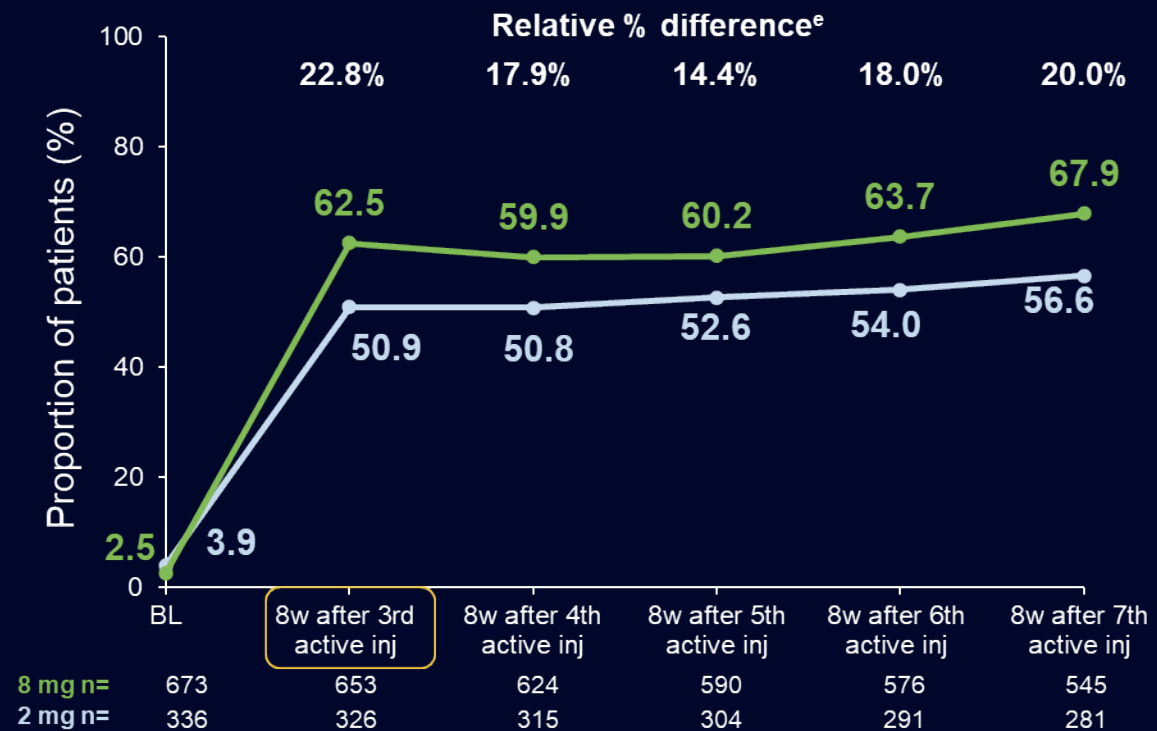
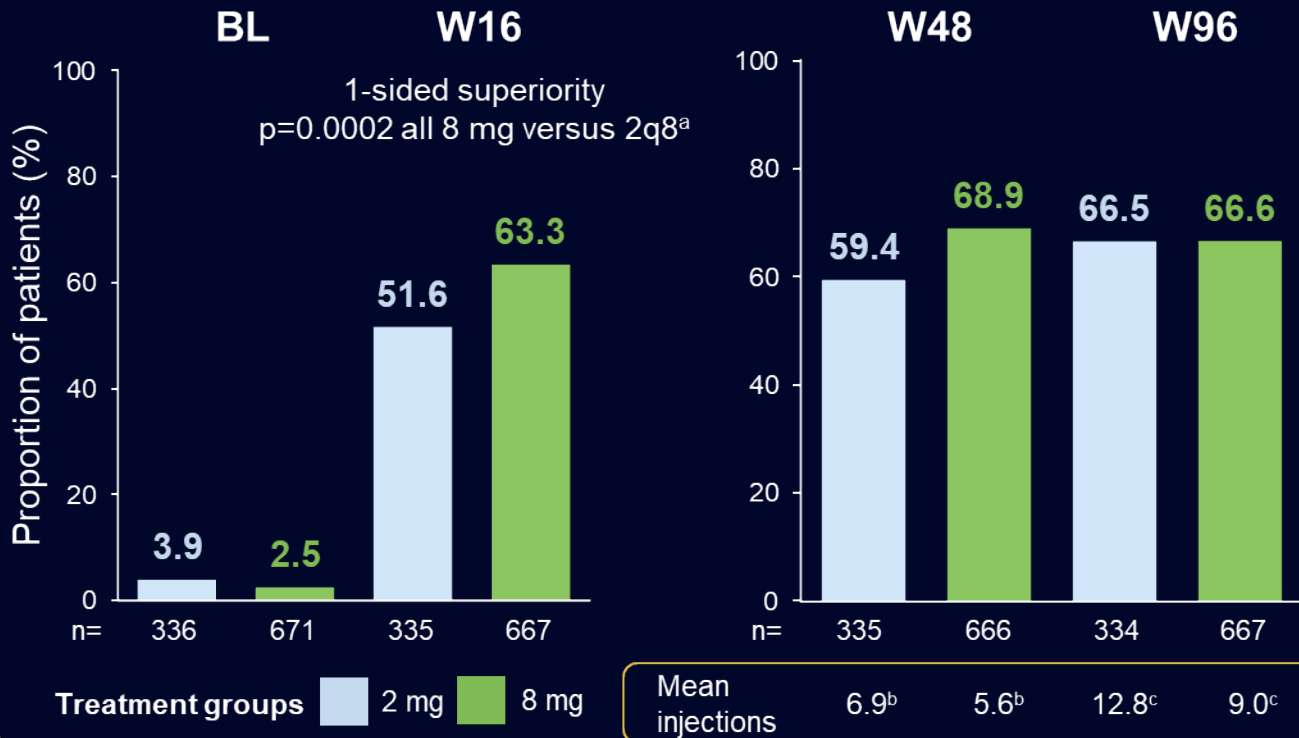
Proportion of Patients Without Retinal Fluid in Center Subfield



Rapid and superior fluid control with 8 mg after monthly initial injections

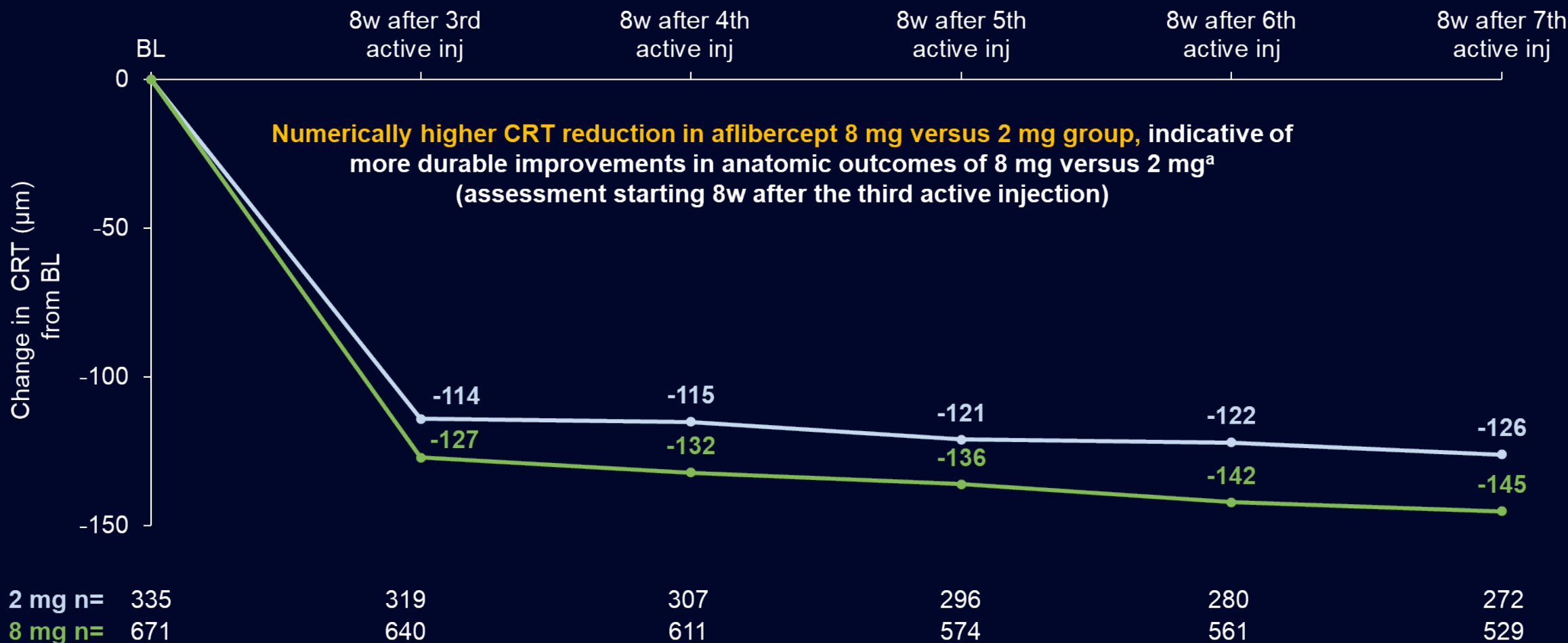
Resilient fluid control at Y1 and Y2 with fewer injections for 8 mg versus 2q8

Matched timepoints^d:
14–23% higher fluid resolution with 8 mg versus 2 mg^e when fluid was assessed 8w after each active injection^f (assessment starting 8w after the third active injection)



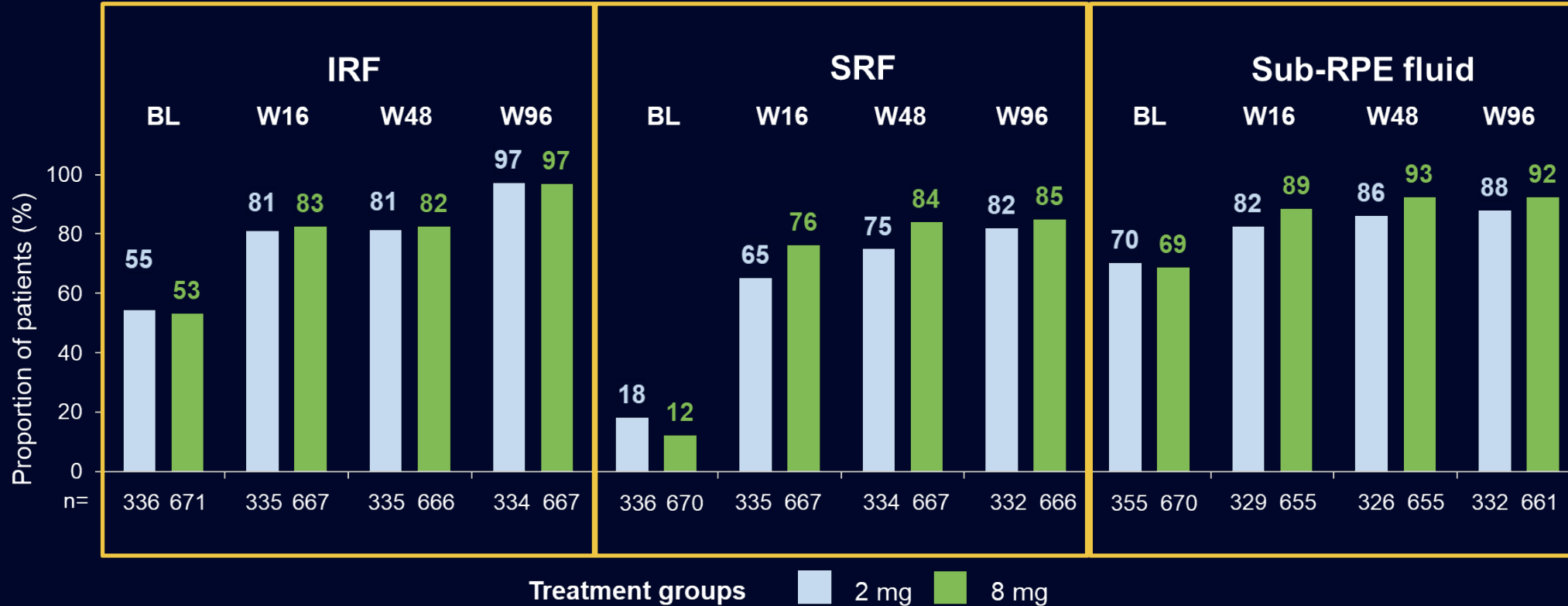
FAS, LOCF (censoring data post ICE); FAS: 2q8 n=336; 8q12 n=335; 8q16 n=338; all 8 mg n=673. The absence of retinal fluid was defined as no IRF and no SRF in center subfield. ^aP-value: 1-sided CMH; weighting scheme adjusted by geographic region and BL BCVA (<60 vs ≥60); ^bPatients completing Week 48; ^cPatients completing Week 96; ^dOC, FAS. OC prior to ICE adjusted by geographic region and BL BCVA (<60 vs ≥60); visits were matched such that patients in any treatment group received the same number of active injections; ^eDifference between absolute percentages in the 8 mg and 2 mg group divided by the percentages in the 2 mg group; ^fWith an interval of ≥8w afterwards. 8w, 8 weeks; CMH, Cochran-Mantel-Haenszel; inj, injection; IRF, intraretinal fluid; LOCF, last observation carried forward; OC, observed cases; SRF, subretinal fluid; Y, year.

Matched Timepoints: CRT Change from Baseline



OC, FAS. OC prior to ICE adjusted by geographic region and baseline BCVA (<60 vs ≥60). Visits were matched such that patients in any treatment group received the same number of active injections.
^aWith an interval of ≥8w afterwards.

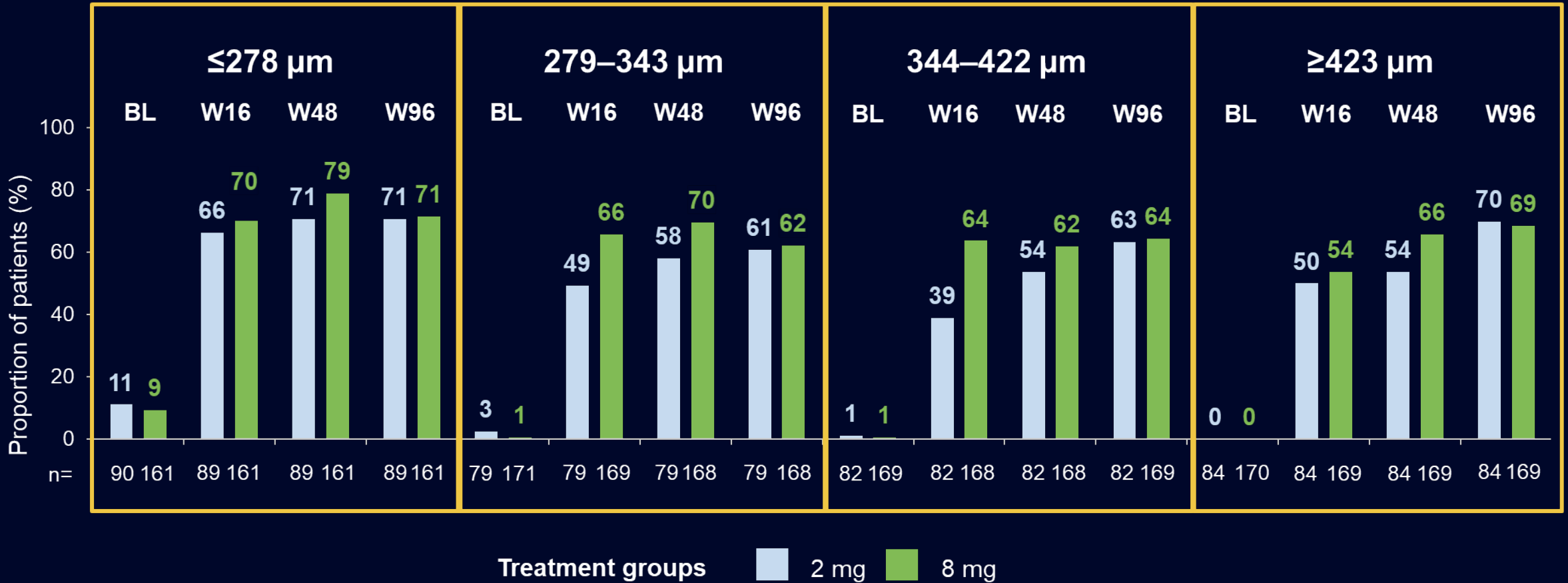
Proportion of Patients Without IRF, SRF, and Sub-RPE Fluid in the Center Subfield At Weeks 16, 48, and 96



- Fluid control was maintained from Week 16 to Week 96 for all fluid types
- The proportion of patients without each fluid type was comparable with 2 mg vs 8 mg with fewer injections at Week 96

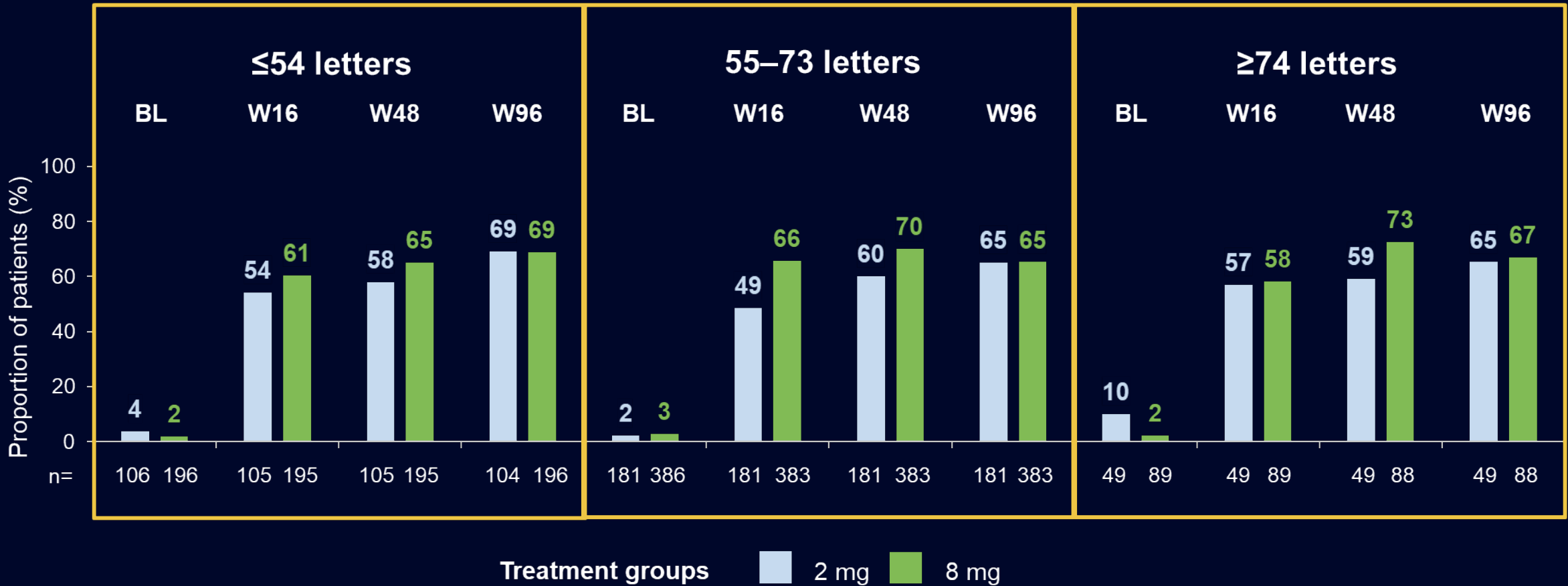
FAS, LOCF prior to ICE was used to impute missing data.
sub-RPE, subretinal pigment epithelium.

Proportion of Patients Without Fluid in the Center Subfield at Weeks 16, 48, and 96 Stratified by Baseline CRT



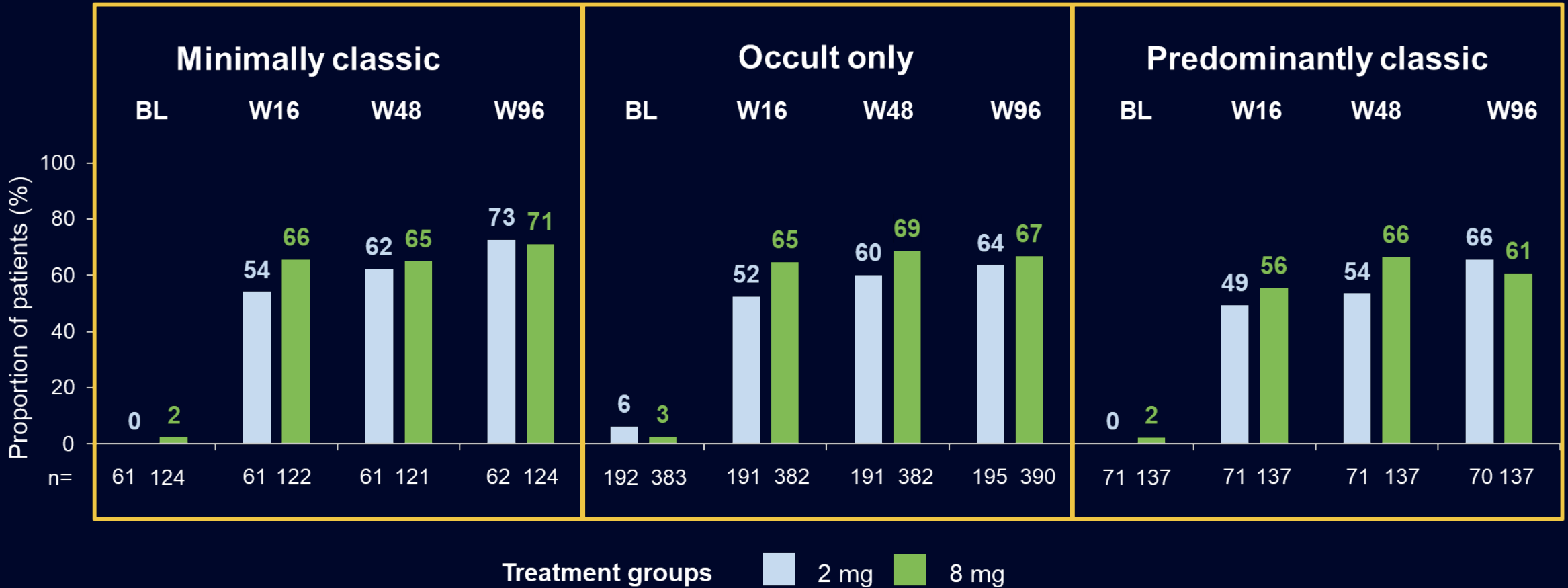
- Fluid control was maintained from Week 16 to Week 96 for all baseline CRT subgroups
- Regardless of baseline CRT, the proportion of patients without retinal fluid was comparable with aflibercept 2 mg versus 8 mg with fewer injections at Week 96

Proportion of Patients Without Fluid in the Center Subfield at Weeks 16, 48, and 96 Stratified by Baseline BCVA



- Fluid control was maintained from Week 16 to Week 96 for all baseline BCVA subgroups
- Regardless of baseline BCVA, the proportion of patients without retinal fluid was comparable with aflibercept 2 mg versus 8 mg with fewer injections at Week 96

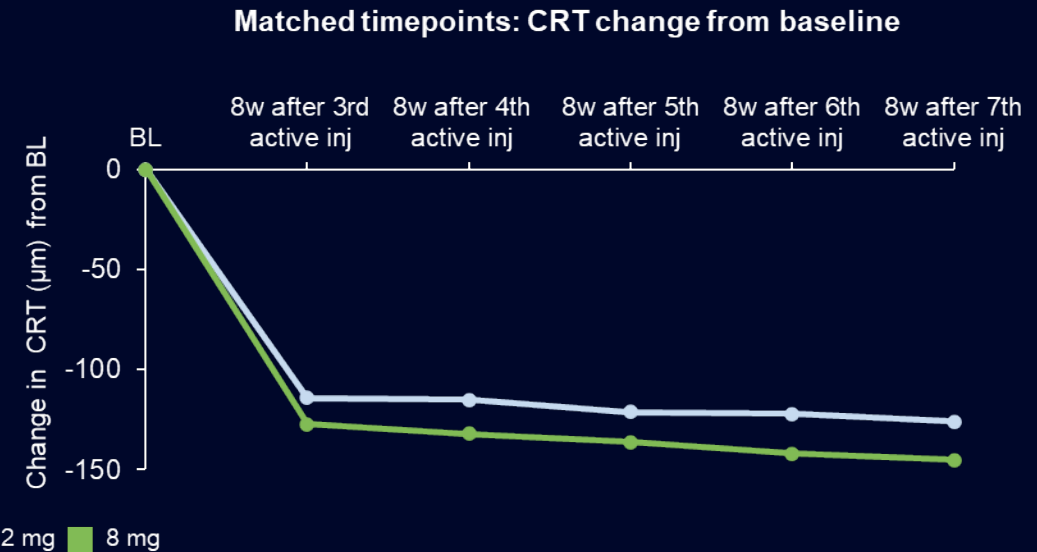
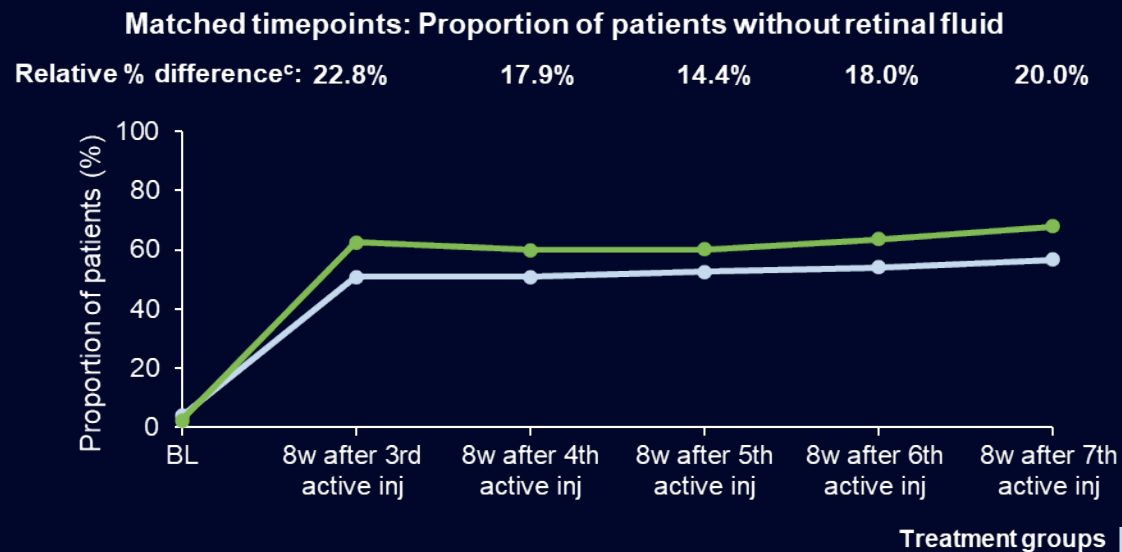
Proportion of Patients Without Fluid in the Center Subfield at Weeks 16, 48, and 96 Stratified by Baseline CNV Type



- Fluid control was maintained from Week 16 to Week 96 for all baseline CNV-type subgroups
- Regardless of baseline CNV type, the proportion of patients without retinal fluid was comparable with aflibercept 2 mg versus 8 mg with fewer injections at Week 96

Conclusions

- The observed data show that **resilient fluid control** is achievable at 1 and 2 years **with fewer injections for aflibercept 8 mg versus 2 mg** in a substantial proportion of patients with treatment-naïve nAMD with extended dosing intervals^a
- Fluid control was maintained** from Week 16 to Week 96 for all baseline subgroups, and regardless of disease severity, the **proportion of patients without retinal fluid was comparable for aflibercept 2 mg vs 8 mg with fewer injections** through Week 96
- 14–23% **higher fluid resolution** was observed with 8 mg versus 2 mg when fluid was assessed 8 weeks after each active matched injection, starting from the third injection^b



OC, FAS. OC prior to ICE adjusted by geographic region and BL BCVA (<60 vs ≥60). ^a6.9 versus 5.6 injections at Week 48, and 12.8 versus 9.0 injections at W96 in the aflibercept 8 mg versus 2 mg groups, respectively; ^bVisits were matched such that patients in any treatment group received the same number of active injections. Assessment starting 8 weeks after the third active injection; ^cDifference between absolute percentages in the 8 mg and 2 mg group divided by the percentages in the 2 mg group.