Visual and anatomical outcomes by q12w/q8w status in the HAWK and HARRIER studies of brolucizumab versus aflibercept in neovascular age-related macular degeneration

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Disclosures

Peter K. Kaiser
- Aerie, Aerpio, Alcon, Allegro, Allergan, Alzheon, Annexon Biosciences, AsclepiX, Bayer, Bausch + Lomb, Biogen Idec, Boehringer Ingelheim, Carl Zeiss Meditec, Clearside Biomedical, Eyevensys, Formycon/BioEq GmbH, Galecto Biotech, Galimedix, Glaukos, Innovent, iRenix, jCyte, Kala Pharmaceuticals, Kanghong, Kodiak, NGM Biopharmaceuticals, Inc., Novartis, Ocugenix, Oculis, Omeros, Opthea, Oxurion, Palatin, Regeneron, RegenxBio, Retinal Sciences, Roivant, Sandoz, Santen, SciFluor, Spark, Stealth Biotherapeutics, Takeda, Thea, Verana

Frank G. Holz
- Grants: Bayer, Centervue, Genentech/Roche, Heidelberg Engineering, Novartis, Zeiss; Consultant: Acucela, Alcon, Bayer, Boehringer-Ingelheim, Galimedix, Genentech, Heidelberg Engineering, Lin-Bioscience, Khanghong, Oxurion, Novartis, Roche, Zeiss

Adrian Koh
- Consultancy fees and honoraria from Novartis

Yuichiro Ogura
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Glenn J. Jaffe
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Ramin Tadayoni
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Ursula Schmidt-Erfurth
- Consultant for Genentech, Heidelberg Engineering, Kodiak, Novartis, RetInSight, Roche

Julie Clark
- Employee of Novartis Pharma AG at time of study

Carrie Murray
- Employee of Novartis Pharma AG at time of study

Kinfemichael Gedif
- Employee of Novartis Pharma AG

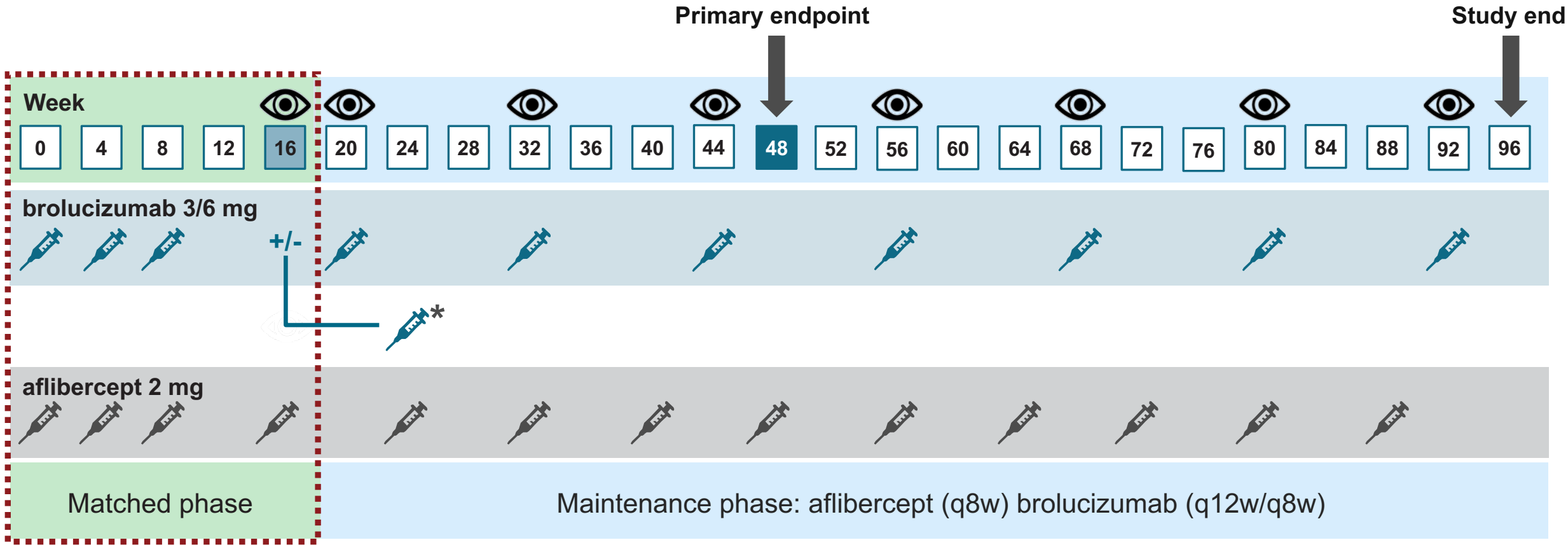
Pravin Dugel
- Acucela, Aerpio, Alcon Pharmaceutical, Alcon Surgical, Alimera Sciences, Allergan, AMO, Annidis, ArcticDX, Avalanche, Bausch + Lomb Pharma, ByeOnics, CDR-Life Inc, Chengdu Kanghong Biotechnology, Clearside Biomedical, Digisight, DOSE Medical, Genentech, Graybug Vision, Irenix, Lutronic, Lux BioScience, MacuSight, NeoVista, Neurotech, Novartis, Omeros, Opthea, Ophthotech, Optovue, ORA, Orbis International, PanOptica, Pentavision, Roche, Santen Inc, SciFluor Life Sciences, Shire Human Genetics, Stealth Biotherapeutics, Thrombogenics, TopCon, TrueVision

Summary

- HAWK and HARRIER: brolucizumab q12w/q8w met the primary endpoint of non-inferiority to aflibercept q8w in BCVA change from baseline to Week 48; BCVA gain was maintained through Week 96
- Brolucizumab subgroups with lesser or greater treatment need were identified based on masked investigators' disease assessments
- Further analyses to compare brolucizumab and aflibercept-treated eyes with lesser or greater treatment need were conducted by applying equal criteria
  - Similar BCVA outcomes were seen for brolucizumab- and aflibercept-treated eyes with greater treatment need to the primary endpoint at Week 48, with a numerical advantage for brolucizumab towards Week 96; greater CST reductions were observed for brolucizumab versus aflibercept
  - BCVA and CST outcomes were comparable for brolucizumab- and aflibercept-treated eyes with lesser treatment need, with most brolucizumab patients on a q12w regimen

BCVA, best-corrected visual acuity; CST, central subfield thickness; q8w, 8-week dosing interval; q12w, 12-week dosing interval

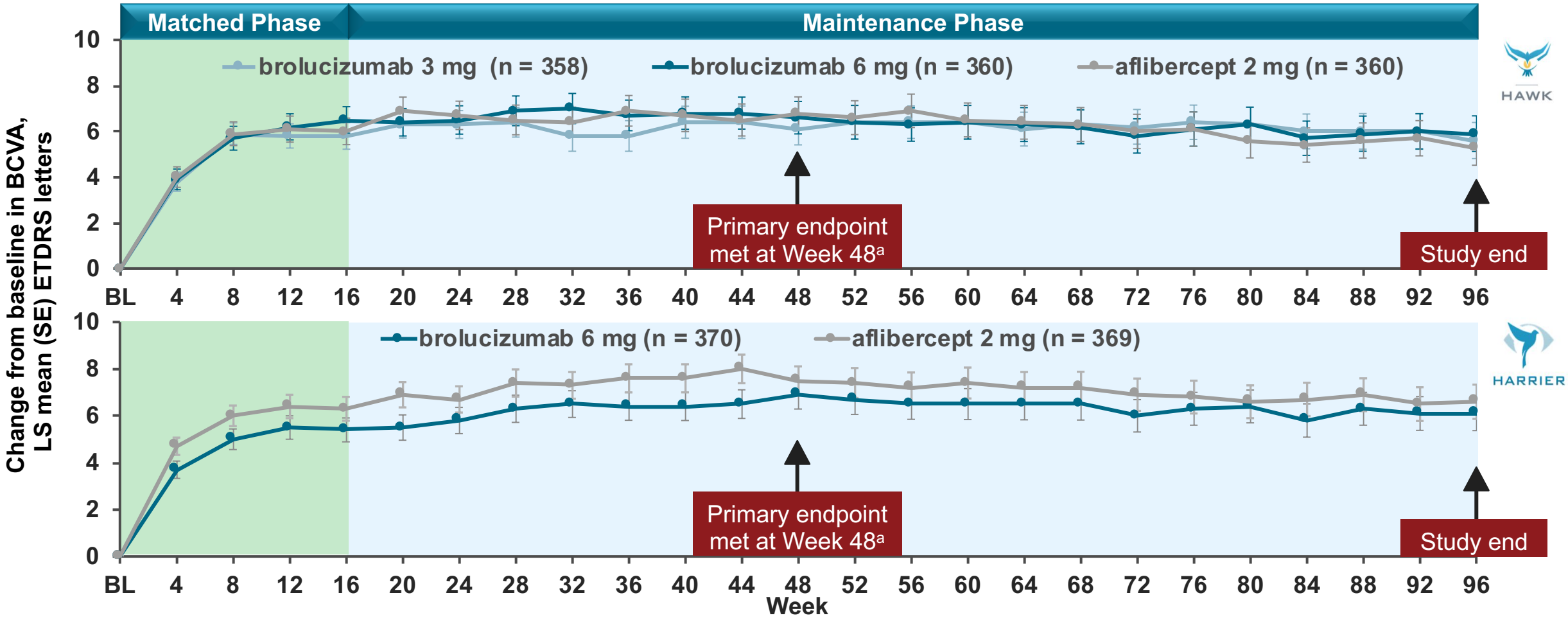
HAWK and HARRIER: brolucizumab (q12w/q8w) vs aflibercept (q8w)[1,2]



Disease activity assessment by masked investigators[a]
*If disease activity was detected at any DAA visit, patients on brolucizumab q12w were adjusted to, and remained on, a q8w regimen

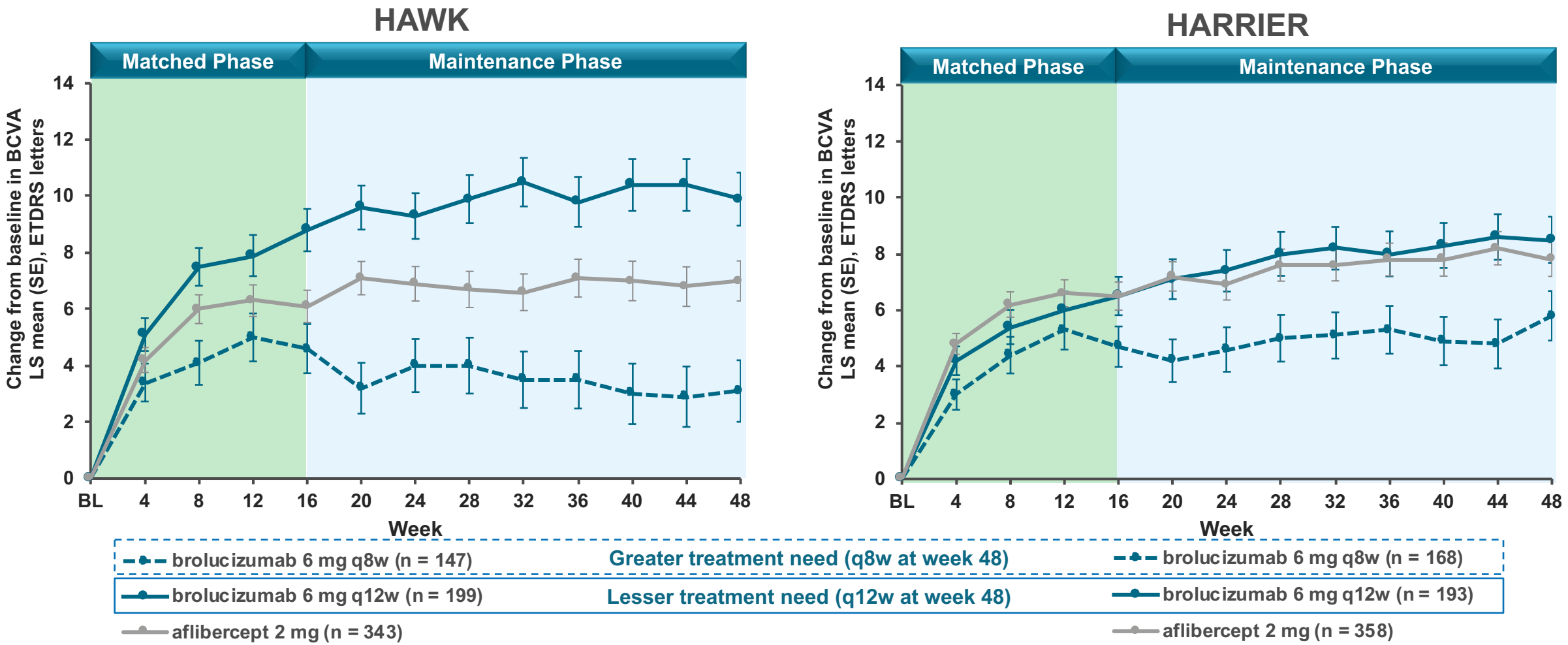
1. Dugel PU, et al. Ophthalmology 2020;127:72; 2. Dugel PU, et al. Ophthalmology 2020 doi: 10.1016/j.ophtha.2020.06.028. [Epub ahead of print]
[a]Disease activity assessments were conducted at pre-specified visits by the masked investigator. Presence of disease activity was determined at the discretion of the masked investigator and supported by protocol guidance based on dynamic functional and anatomical characteristics. Additional assessments and potential dosing interval adjustments occurred at Weeks 28, 40, 52, 64, 76, and 88 in HARRIER only. Sham injections were administered to maintain masking. Visual and anatomic assessments were made prior to injections at Weeks 16 and 48. DAA, disease activity assessment; q8w, 8-week dosing interval; q12w, 12-week dosing interval

BCVA change from baseline to Week 96: brolucizumab versus aflibercept[1,2]



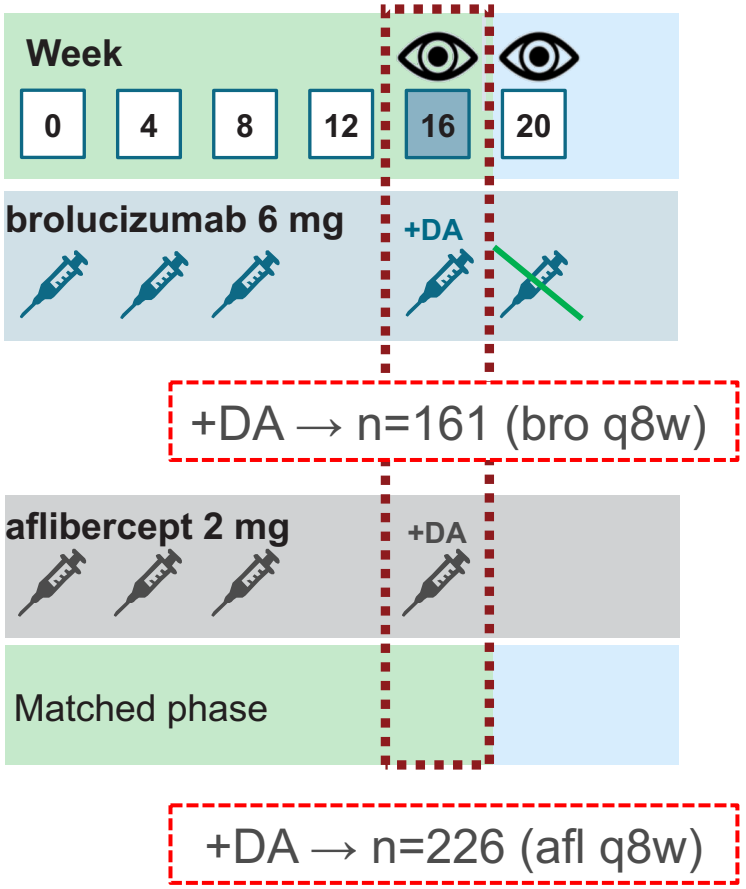
1. Dugel PU, et al. Ophthalmology 2020;127:72; 2. Dugel PU, et al. Ophthalmology 2020 doi: 10.1016/j.ophtha.2020.06.028. [Epub ahead of print]
Full Analysis Set, LOCF. [a]Non-inferiority (NI) margin = 4 letters. Analyzed using ANOVA model with baseline BCVA categories (≤55, 56–70, ≥71 letters), age categories (<75, ≥75 years) and treatment as fixed effect factors.
BCVA, best corrected visual acuity; BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study. LOCF, last observation carried forward; LS, least squares; SE, standard error

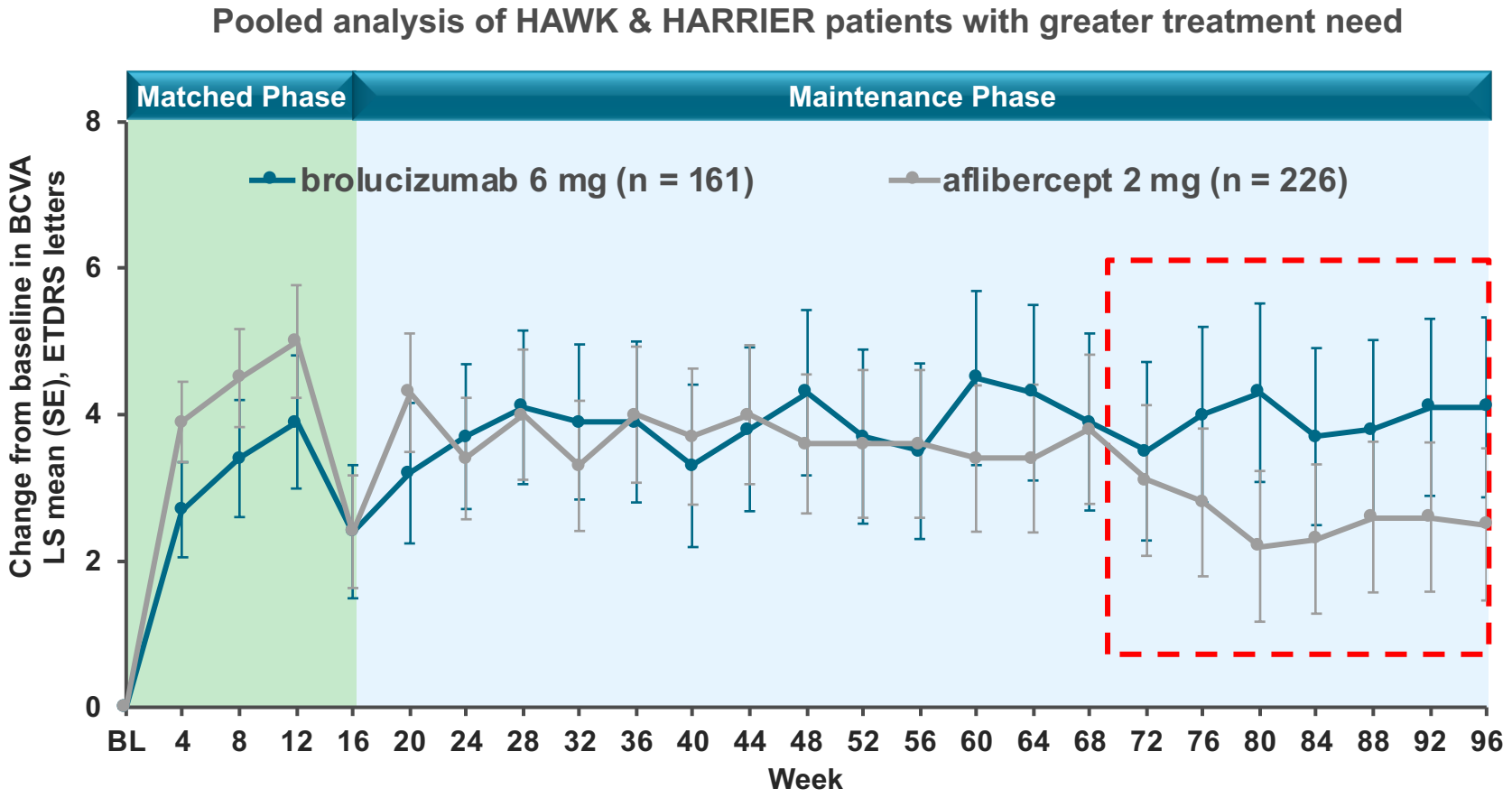
BCVA change from baseline by brolucizumab 6 mg q12w or q8w dosing at Week 48



Full Analysis Set, LOCF. LS mean and SE estimates are based on an ANOVA model with baseline BCVA (≤55, 56–70, ≥71 letters), age (<75, ≥75 years), and treatment as fixed effect factors. BCVA assessments after start of alternative anti-VEGF treatment in the study eye are censored and imputed by the last value prior to start of this alternative treatment. Only subjects with at least one disease activity assessment are included. q12 = subjects with no identified q8 need by the investigator up to Week 48; q8 = subjects with at least one identified q8 need by the investigator up to Week 48. BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; LOCF, last observation carried forward; LS, least squares; q8w, 8-week dosing interval; q12w, 12-week dosing interval; SE, standard error; VEGF, vascular endothelial growth factor

BCVA change from baseline to Week 96: eyes with DA at Week 16 as assessed by investigators





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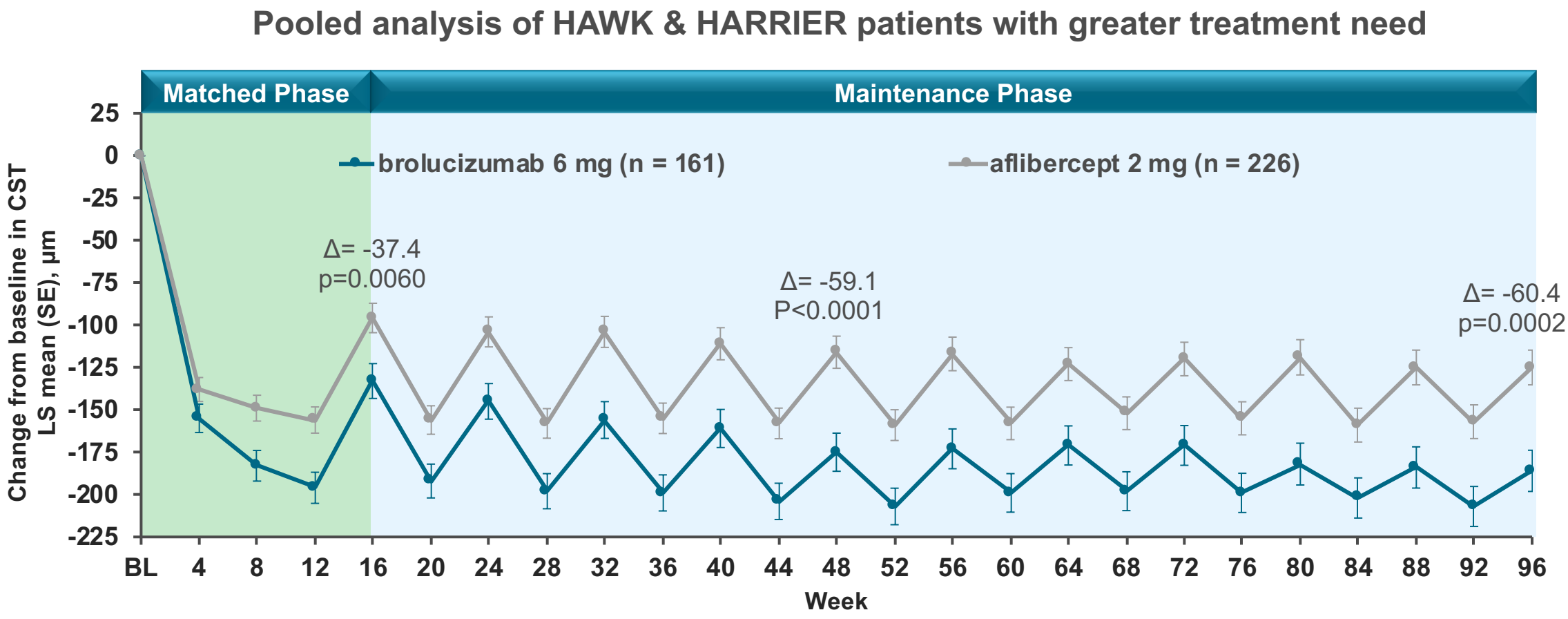
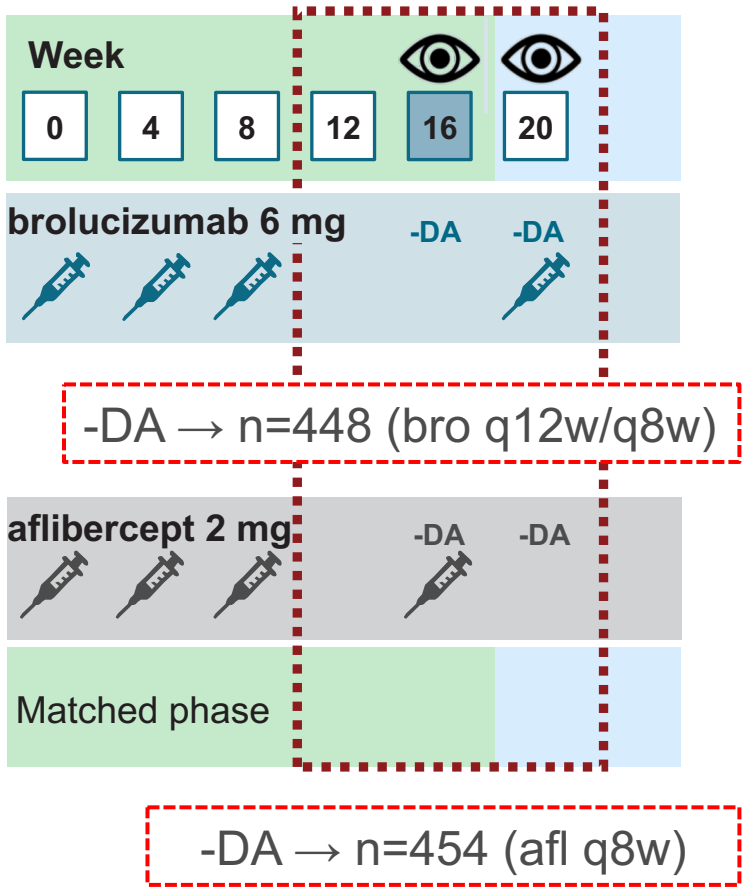
CST change from baseline to Week 96: eyes with DA at Week 16 as assessed by investigators

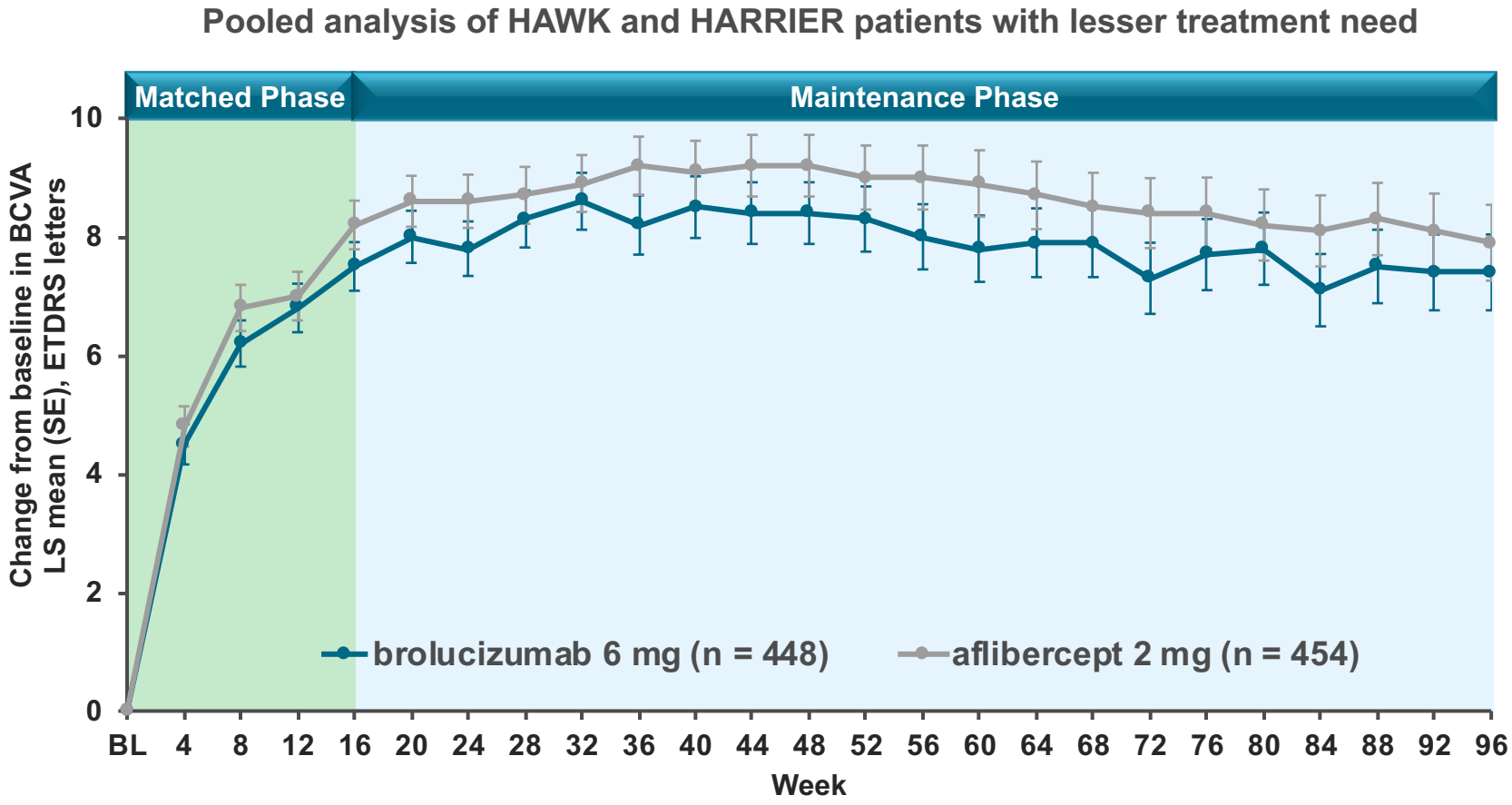


Full Analysis Set, LOCF. LS mean and SE estimates are based on an ANOVA model with baseline CST-total (<400, ≥400 µm), age (<75, ≥75 years) and treatment as fixed effect factors. CST assessments after start of alternative anti-VEGF treatment in the study eye are censored and imputed by the last value prior to start of this alternative treatment.

CST, central subfield thickness; DA, disease activity; LS, least squares; SE, standard error; VEGF, vascular endothelial growth factor

BCVA change from baseline to Week 96: eyes without DA at Weeks 16 and 20 as assessed by investigators





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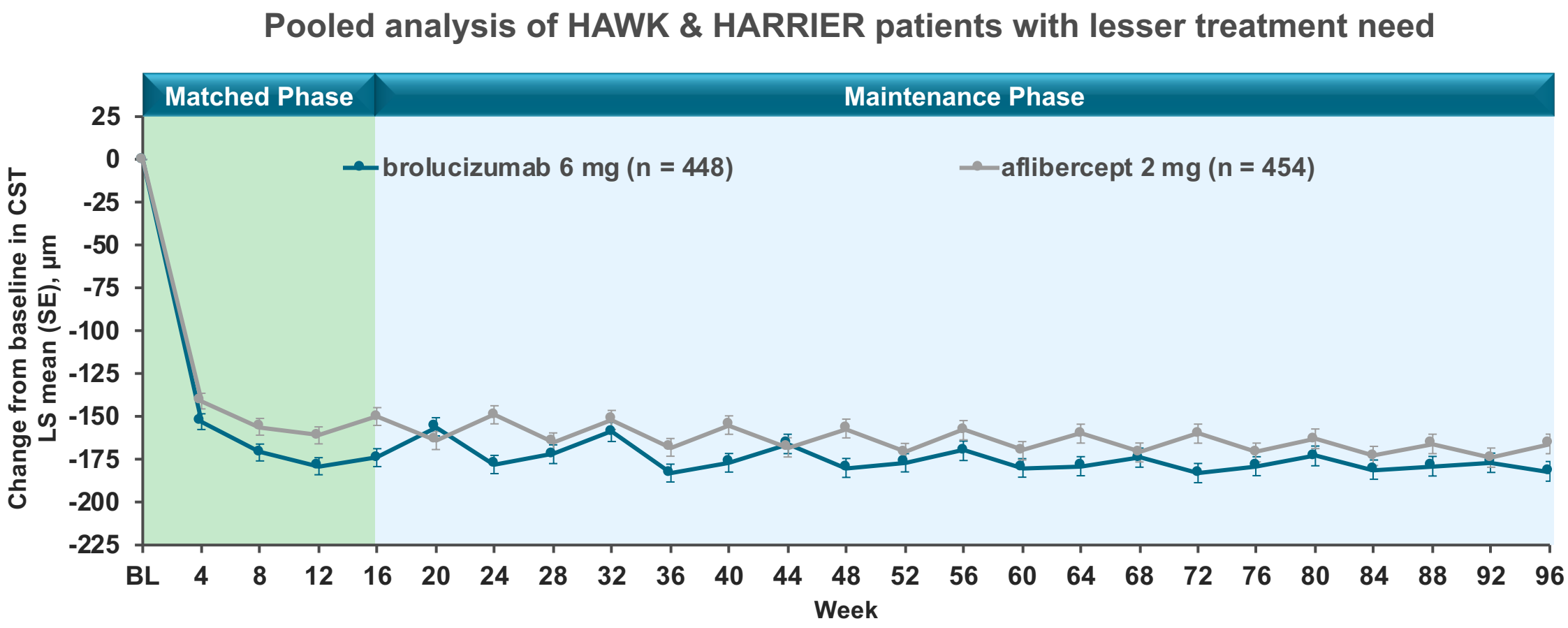
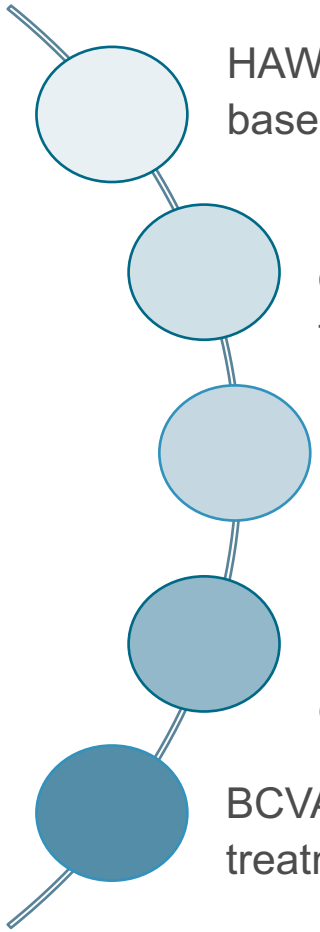
CST change from baseline to Week 96: eyes without DA at Weeks 16 and 20 as assessed by investigators



Full Analysis Set, LOCF. LS mean and SE estimates are based on an ANOVA model with baseline CST-total (<400, ≥400 µm), age (<75, ≥75 years) and treatment as fixed effect factors. CST assessments after start of alternative anti-VEGF treatment in the study eye are censored and imputed by the last value prior to start of this alternative treatment.

CST, central subfield thickness; DA, disease activity; LS, least squares; SE, standard error; VEGF, vascular endothelial growth factor

Conclusions



HAWK and HARRIER: brolucizumab q12w/q8w non-inferior to aflibercept q8w in BCVA change from baseline to Week 48

Difference in BCVA change at Week 48 between brolucizumab q12w and q8w subgroups, based on masked investigators' assessment of DA, reflects disease profiles with lesser or greater treatment need

Higher overall proportion of aflibercept- versus brolucizumab-treated eyes had DA at Week 16

Comparable BCVA outcomes for brolucizumab and aflibercept-treated eyes with greater treatment need from baseline to Week 96, with a numerical advantage for brolucizumab towards Week 96; greater CST reductions for brolucizumab versus aflibercept

BCVA and CST results comparable for brolucizumab and aflibercept-treated patients with lesser treatment need, with most brolucizumab patients on q12w regimen

BCVA, best-corrected visual acuity; CST, central subfield thickness; DA, disease activity; q8w, 8-week dosing interval; q12w, 12-week dosing interval