

A comparison of the efficacy of brolucizumab and aflibercept in eyes with early persistent retinal fluid: 96–week results from the HAWK and HARRIER studies



David R. Lally^{1,2}, Anat Lowenstein³, Jennifer J. Arnold⁴, Yit C. Yang⁵, Kinfemichael Gedif⁶, Catherine Best⁷, Hersh Patel⁸, Ramin Tadayoni⁹ and Jeffrey S. Heier¹⁰

1 New England Retina Consultants, Massachusetts, USA; 2 Department of Surgery, University of Massachusetts Medical School-Baystate, Springfield, Massachusetts, USA; 3 Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; 4 Marsden Eye Specialists, Parramatta, New South Wales, Australia; 5 Royal Wolver Hampton Hospitals NHS Trust, UK; 6 Novartis Pharmaceuticals Corporation, Fort Worth, Texas; 7 Novartis Pharma AG, Basel, Switzerland; 8 Novartis Pharmaceutical Corporation, East Hannover, USA; 9 Université de Paris, Ophthalmology Department, AP-HP, Hôpital Lariboisière, F-75010, Paris, France; 10 Ophthalmic Consultants of Boston, Massachusetts, USA

Retina Society Annual Meeting, September 2020

Financial Disclosures

David R. Lally: Aldeyra Therapeutics, Alimera Sciences, Allergan, Apellis, Canon, Chengdu Kanghong, Emmes/MacTel Project, Genentech, Iveric Bio, Kodiak Sciences, Kubota Vision, Novartis, Neurotech, Notal Vision, Optos, Stealth Biotherapeutics

Anat Lowenstein: Consultant to Allergan, Bayer HealthCare, BeyeOnics Surgical, ForSightlabs, Notal Vision, Novartis and Roche

Jennifer J. Arnold: Honoraria from Allergan, Bayer, Alcon and Novartis

Yit C. Yang: Receipt of honoraria, travel reimbursement, patent royalties from Alcon, Allergan, Alimera Sciences, Bayer, Novartis, Pfizer, Thrombogenics, Heidelberg and Roche

Kinfemichael Gedif: Employee of Novartis Pharmaceuticals Corporation, Fort Worth, Texas

Catherine Best: Employee of Novartis Pharma AG, Switzerland

Hersh Patel: Employee of Novartis Pharmaceutical Corporation, East Hannover, USA

Ramin Tadayoni: Alcon, Baush and Lomb, FCI, Moria, Zeiss, Optovue, Topcon, Alimera, Allergan, Bayer, Novartis, Oculis, Genentech, Roche, Thea

Jeffrey S. Heier: Scientific advisory fees from 4DMT, Adverum, Aerie, Aerpio, Aldeyra, Alkahest, Allegro, Allergan, Annexon, Apellis, Array, Asclepix, BVI, Eloxx, Galimedix, Genentech, Generation Bio, Gyroscope, Interface, iRenix, Janssen R&D, jCyte, Kala, Kanghong, Kodiak, NGM, Notal Vision, Novartis, Ocugenix, Oculis, Ocular Therapeutix, Omeicos, Regeneron, Regenxbio, Retrotope, Santen, Scifluor, Shire, Stealth Biotherapeutix, Tyrogenex, Voyant; research funding from Aerpio, Apellis, Clearside, Genentech, Genzyme, Gyroscope, Hemera, Janssen, jCyte, KalVista, Kanghong, Novartis, Ophthotech, Regeneron, Regenxbio, Stealth, Thrombogenics, TLC

Introduction



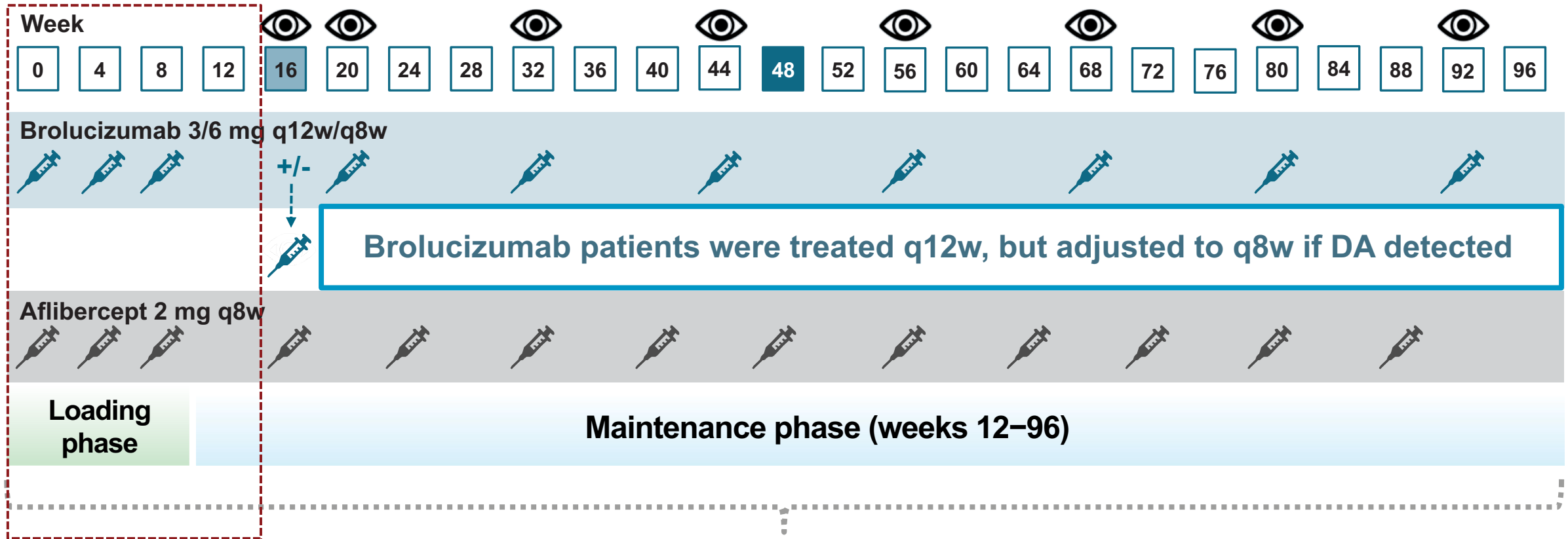
The reduction of retinal fluid is a hallmark of anti-vascular endothelial growth factor (VEGF) treatment for patients with neovascular age related macular degeneration (nAMD)



A subgroup of patients have persistent retinal fluid despite monthly treatment with anti-VEGF injections

The aim of current analysis is to compare the outcomes of brolocizumab 6 mg and aflibercept 2 mg treatment on best-corrected visual acuity (BCVA) and central subfield thickness (CST) in patients with early persistent retinal fluid from HAWK and HARRIER

HAWK and HARRIER: Study Design



Brolucizumab patients were treated q12w, but adjusted to q8w if DA detected

The subgroups for current analysis were defined post randomization based on patient response to treatment (IVT – Brolucizumab/Aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12

Disease activity assessment

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 functional and anatomical characteristics. OCT images and BCVA were collected monthly at all visits. 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. DA, disease activity; IVT, intravitreal; q8w, 8-week dosing interval; q12w, 12-week dosing interval

Dugel PU et al. HAWK and HARRIER: 96-Week outcomes from the phase 3 trials of brolucizumab for neovascular age-related macular degeneration; Ophthalmology; published online June 2020

Methodology

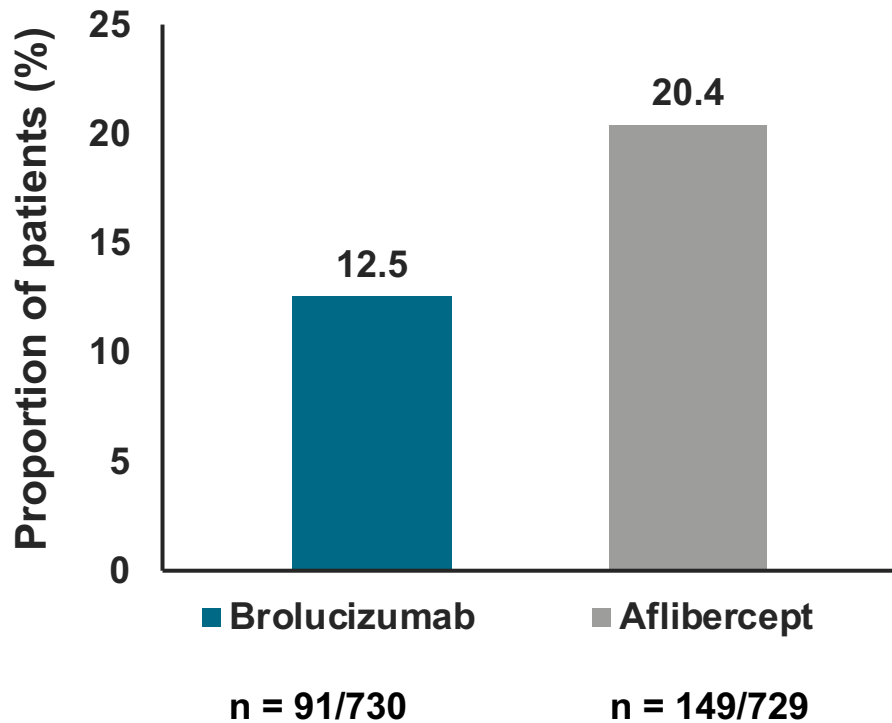


- Early persistent retinal fluid was defined as presence of Sub-Retinal Fluid (SRF) and/or Intra-Retinal Fluid (IRF) at Baseline, Week 4, Week 8 and Week 12
- Differences in BCVA and CST outcomes between brolocizumab 6 mg and aflibercept 2 mg patients from the **pooled** HAWK and HARRIER data were analyzed using ANOVA model with baseline BCVA/CST and age categories as covariates

Population and baseline characteristics of patients with early persistent retinal fluid



Proportion of patients with early persistent retinal fluid



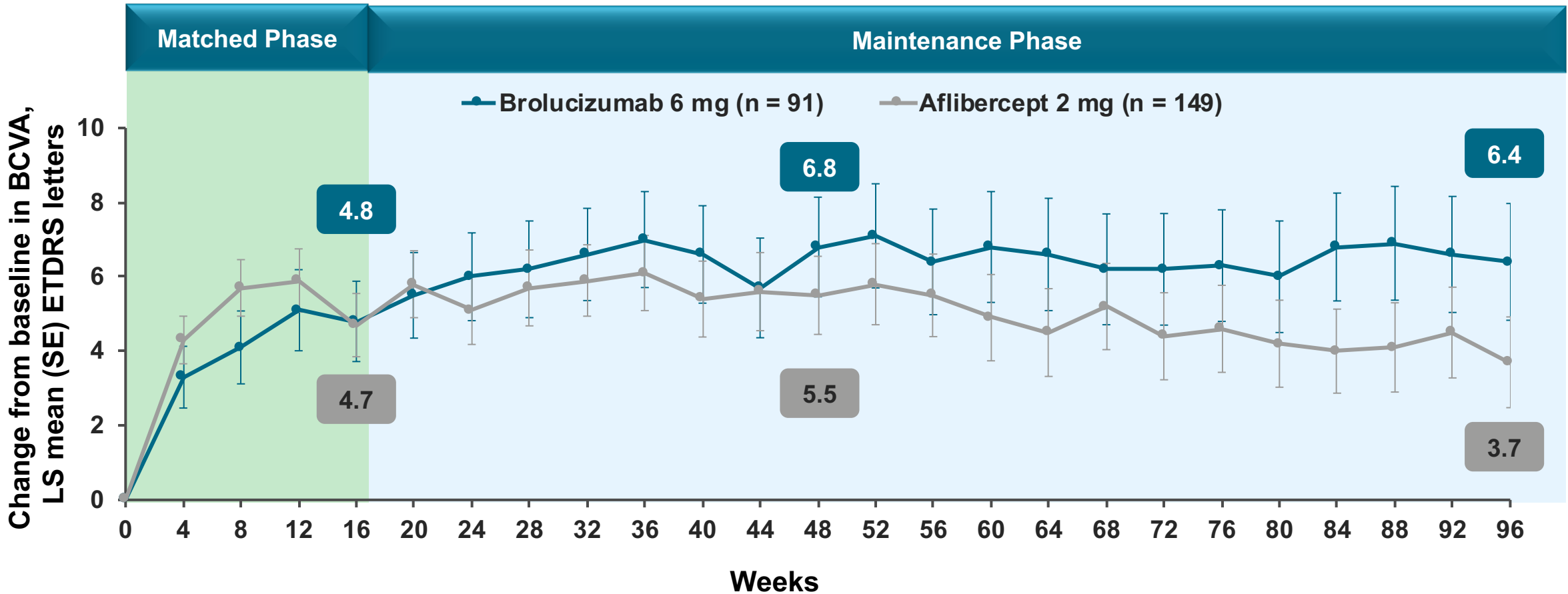
Baseline characteristics of patients with early persistent retinal fluid were well balanced in both groups

Characteristic	Brolucizumab 6 mg	Aflibercept 2 mg
Number of patients, n	91	149
Mean age, years	75	75
Sex		
Female (%)	49.5 %	44.3 %
Mean baseline BCVA, ETDRS letters	54.0	58.7
Mean CST, μm	527.4	483.1

These subgroups (patients with early persistent retinal fluid) are defined post randomization based on patients' response to treatment (IVT – brolucizumab/aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12

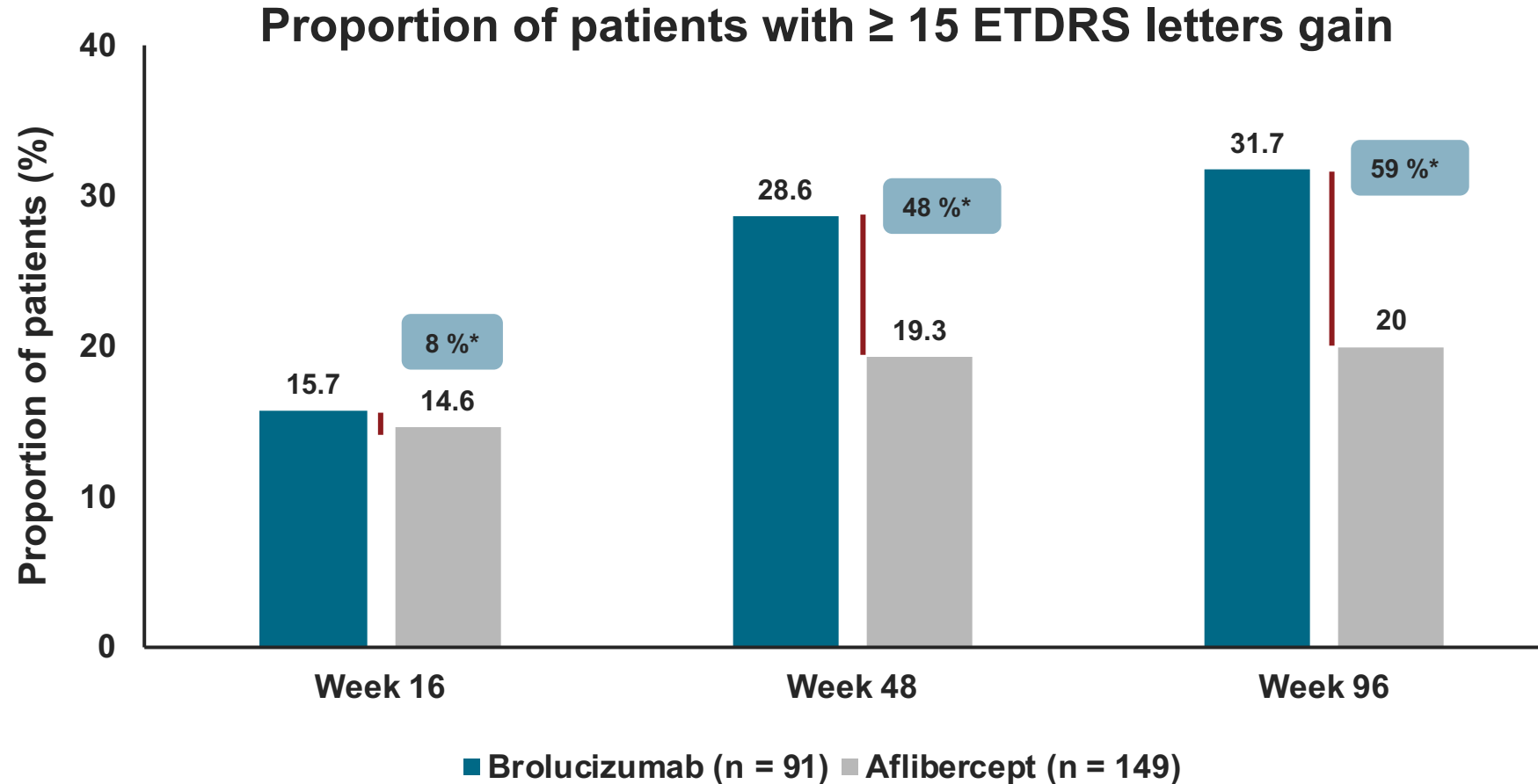
BCVA, best corrected visual acuity; BL, baseline; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; IVT, intravitreal

In patients with early persistent fluid numerically greater BCVA gains were observed with brolucizumab compared with aflibercept



Full Analysis Set, LOCF. Analyzed using ANOVA model with baseline BCVA categories (≤ 55 , 56-70, ≥ 71 letters), age categories (< 75 , ≥ 75 years) and treatment as fixed effect factors. These subgroups (patients with early persistent retinal fluid) are defined post randomization based on patients' response to treatment (IVT – brolucizumab/aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12. BCVA, best corrected visual acuity; BL, baseline; ETDRS, Early Treatment Diabetic Retinopathy Study. IVT, intravitreal; LOCF, last observation carried forward; LS, least squares; SE, standard error

Higher proportion of these patients achieved ≥ 15 letters with brolucizumab compared with aflibercept



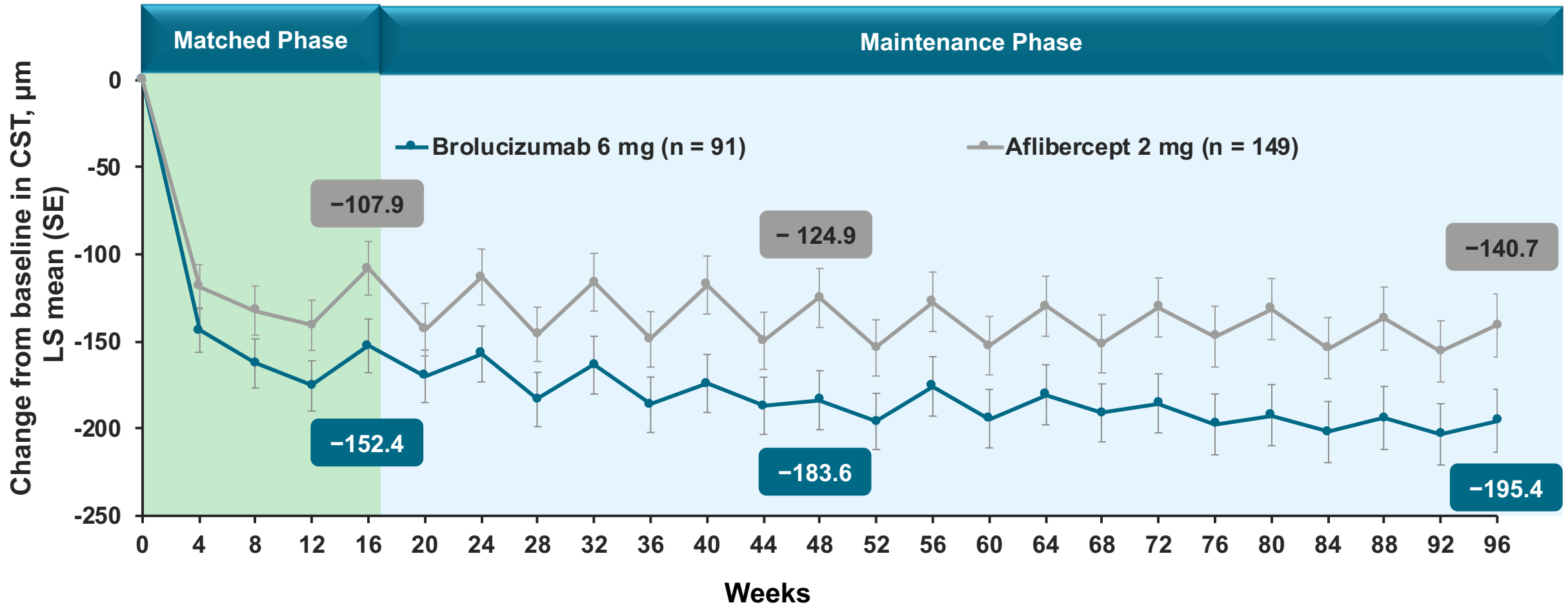
Full Analysis Set, LOCF. Analyzed using ANOVA model with baseline BCVA categories (≤ 55 , 56-70, ≥ 71 letters), age categories (< 75 , ≥ 75 years) and treatment as fixed effect factors.

These subgroups (patients with early persistent retinal fluid) are defined post randomization based on patients' response to treatment (IVT – brolucizumab/aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12

*The percent relative difference in proportion of patients who gained ≥ 15 ETDRS letters is calculated with aflibercept as a reference

EDTRS, early treatment diabetic retinopathy Study. IVT, intravitreal; LOCF, last observation carried forward

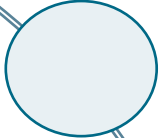
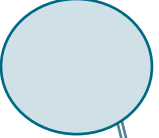
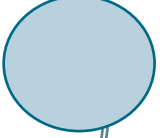
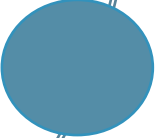

In patients with early persistent fluid brolucizumab achieved greater CST reduction from baseline versus aflibercept



Full analysis set, LOCF. Analyzed using ANOVA model with baseline CSFT-total categories (<400, ≥400 μm), age categories (<75, ≥75 years) and treatment as fixed effect factors. These subgroups (patients with early persistent retinal fluid) are defined post randomization based on patients' response to treatment (IVT – brolucizumab/aflibercept) at baseline, Week 4 and Week 8 and monitoring visit at Week 12
 BL, baseline; CST, central subfield thickness; IVT, intravitreal; LOCF, last observation carried forward; LS, least square; SE, standard deviation

Summary



-  A lower proportion of brolucizumab patients had early persistent retinal fluid compared with aflibercept
-  Patients with early persistent retinal fluid had numerically better BCVA outcomes observed with brolucizumab compared with aflibercept
-  A higher proportion of these patients gained ≥ 15 letters with brolucizumab compared with aflibercept
-  Patients with early persistent retinal fluid had greater CST reductions with brolucizumab compared with aflibercept
-  Brolucizumab may achieve greater disease control in nAMD patients with early persistent retinal fluid than aflibercept