Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

Appendix 1. Study Sites

Diabetic Retinopathy Clinical Research Network clinical sites that participated on this protocol: Sites are listed in order by number of subjects enrolled into the study. The number of subjects enrolled is noted in parenthesis preceded by the site location and the site name. Personnel are listed as (I) for Study Investigator, (C) for Coordinator, (V) Visual Acuity Technician, and (P) for Photographer.

Charlotte, NC Charlotte Eye, Ear, Nose and Throat Assoc., PA (19):
David Browning(I); Omar S. Punjabi(I); Andrew N. Antoszyk(I); Angela K. Price (C,V); Jenna T. Herby (C,V); Taylor S. Jones (C,V); Sherry L. Fredenberg (C,V); Courtney Mahr (C,V); Christina J. Fleming (C,V); Sarah A. Ennis(V); Erica Breglio(V); Angella S. Karow(V); Lisa A. Jackson(P); Uma M. Balasubramaniam(P); Swann J Bojaj(P); Donna McClain(P); Lynn Watson(P); Loraine M. Clark(P); Kathryn Kimrey(P); Jeff A. Kuopus(P); Carol A Simchik(P); Beverly O Rowland(P); Autumn K. Finch(P); Michael D. McOwen(P) **Huntington Beach, CA Atlantis Eye Care (18):** Hani Salehi-Had(I); Sara Ahmed(C); Amy L. Khodai(C); Stephanie Ramirez (C,V); Michael J. Mireles(C); Mary Ma(V); Scott F. Lee(V); Monica J. Rivero(P); Lily Castillo(P) **Indianapolis, IN Raj K. Maturi, M.D., P.C. (18):** Raj K. Maturi(I); Ashley M. Harless (C,V); Carolee K. Novak(V); Nicole Ellingwood(P); Lorraine White(P); Alisha Ware(P) **Houston, TX Baylor Eye Physicians and Surgeons (16):** Christina Y. Weng(I); Robert E. Coffee(I); Petros Euthymiou Carvounis(I); Wendy Blacutt(C); Margaret M. Olfson(C); Karri Schuetzle(C); Pejman Hemati (C,V); April Leger(V); Dana B. Barnett(P); Joseph F. Morales(P) **Minneapolis, MN Retina Center, PA (16):** Abdhish R. Bhavsar(I); Jacob M. Jones(I); Geoffrey G. Emerson(I); Joan Dupont (C); Andrea Gilchrist(C); Dave A. Crannick(C); Gaid Gaid(V); Erin C. Kinney(V,P); Hannah N. Schoenecker(P); Alanna C. Evans(V,P); Nora Gould(V); Tonja Scherer(P,V); Denise Vang(P) **Fort Myers, FL National Ophthalmic Research Institute (9):** A. Thomas Ghuman(I); Ashish G. Sharma(I); Paul A. Raskauskas(I); Eileen Knips(C); Cheryl Ryan(C); Cheryl Kiesel(C); Crystal Y. Peters(C); Laura Greenhoe(C); Natalie N. Torres(C); Anita H. Leslie(V); Danielle Dyshanowitz(V); Raymond K. Kiesel(P) **Portland, OR Casey Eye Institute (8):** Steven T. Bailey(I); Christina J Flaxel(I); Thomas S. Hwang(I); Andreas K. Lauer(I); Mitchell Schain (C,V); Shelley A. Hanel(C); Ann D. Lundquist (C,V); Susan K. Nolte(V); Shirley D. Ira(V); Dawn M. Ryan(P); Scott R. Pickell(P);

Peter N. Steinkamp(P); Jordan Barth(P); Chiedozie Ukachukwu(P); Jocelyn T. Hui(P); Chris S Howell(P) **Santa Barbara, CA California Retina Consultants (7):** Dilsher Dhoot(I); Alessandro A. Castellarin(I); Dante J. Pieramici(I); Gina Hong (C,V); Sara Esau (C,V); Erica D. Morasse (C,V); Jack Giust(C); Sarah Fishbein (C,V); Michelle S. Hanna (C,V); Kelly Avery(V); Jerry Smith(V); Aimee Walker(P) **Lakeland, FL Florida Retina Consultants (6):** Scott M. Friedman(I); Nader Moinfar(I); Damanda F. Fagan (C,V); Kimberly A. Williamson (C,V); Katrina L. Dawson(C); Paige N. Walters(P,V); Allen McKinney(P,V) **Augusta, GA Southeast Retina Center, P.C. (5):** Dennis M. Marcus(I); Harinderjit Singh(I); Siobhan O. Ortiz(C); Michele Woodward(C); Amina Farooq(C); Lindsay Allison Foster(P,V); Thomas Bailey(V); Ken Ivey(P) **Baltimore, MD Elman Retina Group, P.A. (5):** Michael J. Elman(I); Henry A. Leder(I); JoAnn Starr(C); Jennifer L. Belz(C); Twyla J Robinson(C); Pamela V. Singletary(V); Amy Thompson(V); Dallas R. Sandler(P,V); Jennifer L. Simmons(V); Perel M. Simpson(V); Teresa Coffey(V); Terri Cain(P); Ashley M. Metzger(P); Peter Sotirakos(P) **Beverly Hills, CA Retina-Vitreous Associates Medical Group (5):** Roger L. Novack(I); David S. Liao(I); Daniel D. Esmaili(I); Kelly Hu(C); Lynn Pham(C); Tammy Eileen Lo(C); Julio Sierra(V); Adam Zamboni(V); Eric G. Protacio(P); Josh Koo(P) **San Antonio, TX Retinal Consultants of San Antonio (5):** Moises A. Chica(I); Calvin E. Mein(I); Lita Kirschbaum(C); Tori R. Moore (C,V); Jaynee Baker(C); Christopher Sean Wienecke(P,V); Clarissa M. Marquez(P); Brenda Nakoski(P); Elaine Castillo(V) **Dubuque, IA Medical Associates Clinic, P.C. (4):** Michael H. Scott(I); Shannon R. Walsh(C); Marcia J. Moyle(P,V); Brenda L. Tebon(P,V) **GRAND RAPIDS, MI Retina Specialists of Michigan (4):** Thomas M. Aaberg(I); Scott J. Westhouse(I); Holly L. Vincent (C,V); Kyle Brandt(C); Kathy L. Karsten(P,V); Shymaa Mohamed(P,V) **Loma Linda, CA Loma Linda University Health Care, Department of Ophthalmology (4):** Joseph T. Fan(I); Lynn L. Huang(I); Michael E. Rauser(I); Liel Marvyn Cerdenio (C,V); Raquel Hernandez (C,V); William H. Kiernan(V); Jesse Knabb(P); Armand Assissini(P) **Seattle, WA University of Washington Medical Center (4):** James L. Kinyoun(I); Gurunadh Atmaram Vemulakonda(I); Kasra Attaran Rezaei(I); Ian P Luttrell(C); Susan A. Rath (C,V); Francy Moses(V); Juli A. Pettingill(V); Brad C. Clifton(P); Ronald C. Jones(P); James D. Leslie(P) **Beachwood, OH Retina Associates of Cleveland, Inc. (3):** Lawrence J. Singerman(I); Joseph M. Coney(I); Jerome P. Schartman(I); David G. Miller(I); Michael A. Novak(I); Susan C. Rath(C); Veronica A. Smith(C); Cecelia Rykena(V); Mary A

Ilc(V); Tia R Drugan(V); Vivian Tanner(V); Kimberly A. DuBois(V); Gregg A. Greanoff(P); John C. DuBois(P); Elizabeth McNamara(P); William B. Amonett(P) **Knoxville, TN Southeastern Retina Associates, P.C. (3):** Joseph M. Googe(I); R. Keith Shuler(I); Nicholas G. Anderson(I); Kristina Oliver(C); Steve Morris(C); Kathy L. Schulz(V); Julie Rauen(V); Jerry K. Whetstone(P); Justin Walsh(V); Sarah M. Oelrich(P); Raul E. Lince(P) **Lubbock, TX Texas Retina Associates (3):** Michel Shami(I); Yolanda Saldivar(C); Brenda K. Arrington(C); Ashaki Meeks(V); Kayla Blair(P); Ginger K. Rhymes(P); Glenn R Gardner(P) **NEW LONDON, CT Retina Group of New England (3):** Nauman A. Chaudhry(I); Emiliya German(C); Alison Fontecchio(V); Heather Casey(V); Justin A. Cocilo(P) **New York, NY MaculaCare (3):** Daniel F. Rosberger(I); Phuntsho Wangmo(C); Sandra Groeschel(C); Sandra Acevedo(V); Yenelda M. Gomez(P,V); Robert Santora(P) **ROCHESTER, NY University of Rochester (3):** David Allen DiLoreto(I); George W. O'Gara(C); Andrea M. Czubinski (C,V); Rebecca K. Gerhart(V); Patricia A. Artman(P); Taylor A. Pannell(P); Brittany S. Richardson(P); Rachel Hollar(P) **Sarasota, FL Sarasota Retina Institute (3):** Melvin Chen(I); Waldemar Torres(I); Peggy A. Jelemensky(C); Tara L. Raphael(V); Mark Sneath(P); Rosa Miller(V); Jim Sherry(P) **Amarillo, TX Southwest Retina Specialists (2):** Ryan B. Rush(I); Glenn R. Gardner(C); Johnathan R. Hawkins(V); Ben Ysasaga(P) **Austin, TX Retina Research Center (2):** Brian B. Berger(I); Saradha Chexal(I); Chirag D. Jhaveri(I); Ryan M. Reid(C); Ivana Gunderson (C,V); Tina A Seidu(C); Boris Corak(P,V); Yong Ren(P) **Boston, MA Joslin Diabetes Center (2):** Paolo S. Silva(I); Corey Westerfeld(I); Christopher Michael Andreoli(I); Jennifer K. Sun(I); Margaret E. Stockman (C,V); Flor M. Flores (C,V); Linette Miranda (C,V); Troy Kieser (C,V); Jerry D. Cavallerano(V); Elizabeth S. Weimann(P); Rita K. Kirby(P); Steve L. Papaconstantinou(P); Kate A. Palitsch(P); Kylie M. Madigan(P); Robert W. Cavicchi(P) **Houston, TX Retina and Vitreous of Texas (2):** Joseph A. Khawly(I); Emmanuel Chang(I); Diana Abdelgani(C); Erica Pineda(V); Debbie Fredrickson(V); Donald K. Lowd(P); Desiree Lopez(P); Jason E. Muniz(P); Colin Blank(P) **Houston, TX Retina Consultants of Houston, PA (2):** Charles C. Wykoff(I); Richard H. Fish(I); David M. Brown(I); James C. Major(I); Tien P. Wong(I); Matthew S. Benz(I); Amy Hutson(C); Jolene Carranza(C); Lauren Epp(C); Meredith Berry(C); Nubia Landaverde(C); Veronica A. Sneed(V); Belinda A. Almanza(V); Rebecca Yee(V); Beau A Richter(P); Eric N. Kegley(P) **Jacksonville, FL University of Florida College of Med., Department of Ophthalmology, Jacksonville Health Science Cent (2):** Sandeep

Grover(I); Kakarla V. Chalam(I); Ghulam Shabbir Hamdani(C); Zimei Zhou (C,V); Kumar Sambhav (C,V) **Mountain View, CA Northern California Retina Vitreous Associates (2):** Rahul N. Khurana(I); Diana Lam(C); Amy Dennis(C); Andrea Gadda(V) **Philadelphia, PA University of Pennsylvania Scheie Eye Institute (2):** Alexander J. Brucker(I); Sheri Drossner (C,V); Jim M. Berger(P); Sara Morales(P) **Portland, OR Retina Northwest, PC (2):** Mark A. Peters(I); Stephanie L. Ho (C,V); Stephen Hobbs (C,V); Amanda C. Milliron(V); Marcia Kopfer(V) **Redlands, CA Retina Consultants of Southern California (2):** Richard D. Pesavento(I); Jacque' Smith(C); Tina Ramirez(P); Jordan Davis(V)
Richmond, VA Retina Institute of Virginia (2): John Stewart O'Keefe(I); Bryan J. Schwent(I); Suzette A. Rosen(C); Melissa A. Tutka(V); Natalie J. Arndt(V); John J. Maziarz(P) **Saint Louis, MO The Retina Institute (2):** Kevin J. Blinder(I); Thomas K. Krummenacher(I); Erika A. Hoehn(C); Maria A. Stuart(V); Diana Reardon(V); George Guevara(P); Jarrod Wehmeier(P); Steve A Schremp(P); Timothy L Wright(P)
Austin, TX Austin Retina Associates (1): Robert W. Wong(I); Peter A. Nixon(I); Phillip V. Le (C,V); Carrie E. Leung(C); Chris A. Montesclaros(C); Jeni L. Leon(C); Codey L. Daus(P)
Sacramento, CA Retinal Consultants Medical Group, Inc. (1): Margaret A. Chang(I); John Brian Reed(I); Kimberlee S. Wong(C); Eric Bair(V) **Salt Lake City, UT Retina Associates of Utah, P.C. (1):** Robert C. Kwun(I); Kirk E. Winward(I); Victoria L. Knudsen(I); Michelle Riley(C); Shauna Ma(C); Teresa Taylor(V); Jason G. Winward(P,V) **Warrenton, VA Virginia Retina Center (1):** Sam E. Mansour(I); Cathy Choyce (C,V); Aissa L. Dirawatun(V,P); Ana Mills(P)

DRCR.net Coordinating Center: Jaeb Center for Health Research, Tampa, FL (staff as of 9/22/2017)**:** Adam R. Glassman (Director and Principal Investigator), Roy W. Beck (Executive Director), Daphne Auza, Alyssa Baptista, Wesley T. Beaulieu, Sharon R. Constantine, Brian B. Dale, Simone S. Dupre, Julie Hay, Meagan L. Huggins, Paula A. Johnson, Brittany Kelly, Danni Liu, Brenda L. Loggins, Shannon L. McClellan, Michele Melia, Isoken Odia, Carrie Preston, Cynthia R. Stockdale, Danielle Stanley

DRCR.net Network Chair: Lee M. Jampol (2013-present), Neil M. Bressler (2006-2012)

DRCR.net Vice Chairs: Carl W. Baker (2011-2013, 2017-present), Chirag Jhaveri (2016 – present), Judy Kim (2015-present), Andrew Antoszyk (2013-2016), Jennifer K. Sun (2012-2014), John A. Wells, III (2013- 2015).

National Eye Institute: Sangeeta Bhargava (2016-current) Eleanor Schron (2009-2015)

Data Safety and Monitoring Committee: Gary Abrams, Deborah R. Barnbaum, Harry Flynn, Kyle D. Rudser, Sangeeta Bhargave, Ruth S. Weinstock, Charles P. Wilkinson, Stephen Wisniewski (Chair, 2016-current), John Connett (Chair, 2003-2015)

Executive Committee: Lloyd Paul Aiello (2002-present; Chair 2002 – 2005), Andrew N. Antoszyk (2009; 2013 - present), Carl W. Baker (2009-present), Roy W. Beck (2002-present), Sangeeta Bhargava (2016-present), Barbra Blodi (2014-present), Neil M. Bressler (2006-present; Chair 2006 - 2008), Susan B. Bressler (2009-Present), Matthew D. Davis (2002-present), Michael J. Elman (2006-present; Chair 2009 and 2012), Frederick L. Ferris III (2002-present), Adam R. Glassman (2005-present), Jeffrey G. Gross (2012-present), Glenn J. Jaffe (2012-present), Lee M. Jampol (2012-present; Chair 2013-present), Chirag D. Jhaveri (2016-present), Judy E. Kim (2015-present), Brandon Lujan (2017-present), Dan Martin (2017-present), Raj K. Maturi (2009-2011, 2013- present), Jennifer K. Sun (2009-present). Prior Members: Eleanor Schron (2009-2015) John A. Wells, III (2012-2015).

Appendix 2. Institutional Review Boards

-Jaeb Center for Health Research IRB
-Joslin Diabetes Center IRB
-University of Washington Medical Center IRB
-University of Pennsylvania Scheie Eye Institute IRB
-Casey Eye Institute IRB
-Loma Linda University Health Care, Department of Ophthalmology IRB
-University of Rochester IRB
-University of Florida College of Med., Department of Ophthalmology, Jacksonville Health Science Center IRB
-Baylor Eye Physicians and Surgeons IRB

eTable 1. Eligibility Criteria

Run-in Phase	
Participants	
Inclusion	Age ≥ 18 years
	Diagnosis of diabetes mellitus (type 1 or type 2)
Exclusion	History of chronic renal failure requiring dialysis or kidney transplant
	A condition that, in the opinion of the investigator, would preclude participation in the study (e.g., unstable medical status including blood pressure, cardiovascular disease, and glycemic control)
	Initiation of intensive insulin treatment (a pump or multiple daily injections) within 4 months prior to randomization or plans to do so in the next 4 months
	Participation in an investigational trial that involved treatment with any drug that has not received regulatory approval for the indication being studied within 30 days of enrollment
	Known allergy to any component of the study drugs (including povidone iodine prep)
	Blood pressure >180/110 (systolic above 180 OR diastolic above 110)
	Myocardial infarction, other acute cardiac event requiring hospitalization, stroke, transient ischemic attack, or treatment for acute congestive heart failure within 1 month prior to enrollment
	Systemic steroid, anti-vascular endothelial growth factor (VEGF) or pro-VEGF treatment within 4 months prior to enrollment or anticipated use during the study
	For women of child-bearing potential: pregnant or lactating or intending to become pregnant within the next 9 months
	Individual is expecting to move out of the area of the clinical center to an area not covered by another clinical center during the next 9 months
Study Eye	
Inclusion	At least 3 injections of anti-VEGF drug (ranibizumab, bevacizumab, or aflibercept) within the prior 20 weeks
	Visual acuity letter score in study eye ≤78 and ≥24 (approximate Snellen equivalent 20/32 to 20/320)
	On clinical exam, definite retinal thickening due to DME involving the center of the macula
	OCT CSF thickness (microns), within 8 days of enrollment: Zeiss Cirrus: ≥290 in women, ≥305 in men; Heidelberg Spectralis: ≥305 in women, ≥320 in men
	Media clarity, pupillary dilation, and individual cooperation sufficient for adequate OCTs
Exclusion	Macular edema is considered to be due to a cause other than diabetic macular edema (DME)
	An ocular condition is present such that, in the opinion of the investigator, visual acuity loss would not improve from resolution of macular edema (e.g., foveal atrophy, pigment abnormalities, dense subfoveal hard exudates, non-retinal condition, etc.)
	An ocular condition is present (other than DME) that, in the opinion of the investigator, might affect macular edema or alter visual acuity during the course of the study (e.g., vein occlusion, uveitis or other ocular inflammatory disease, neovascular glaucoma, etc.)
	Substantial lens or posterior capsule opacity that, in the opinion of the investigator, is likely to be decreasing visual acuity by 3 lines or more (i.e., opacity would be reducing acuity to 20/40 or worse if eye was otherwise normal)
	History of intravitreal anti-VEGF drug within 21 days prior to enrollment
	History of intravitreal or peribulbar corticosteroids within 3 months prior to enrollment
	History of macular laser photocoagulation within 4 months prior to enrollment
	History of panretinal (scatter) photocoagulation (PRP) within 4 months prior to enrollment or anticipated need for PRP in the 6 months following enrollment into run-in phase
	Any history of vitrectomy
	History of major ocular surgery (including scleral buckle, any intraocular surgery, etc.) within prior 4 months or anticipated within the next 6 months following enrollment
	History of cataract extraction within 6 months prior to enrollment or anticipated need for cataract extraction within the study follow-up period
	History of YAG capsulotomy performed within 2 months prior to enrollment
	Exam evidence of external ocular infection, including conjunctivitis, chalazion, or substantial blepharitis

	Intraocular pressure ≥25 mmHg
	History of open-angle glaucoma (either primary open-angle glaucoma or other cause of open-angle glaucoma; note: history of angle-closure glaucoma is not an exclusion criterion).
	History of steroid-induced intraocular pressure elevation that required intraocular pressure (IOP)-lowering treatment
	History of prior herpetic ocular infection
	Exam evidence of ocular toxoplasmosis
	Exam evidence of pseudoexfoliation or any other condition associated with zonular dehiscence or lens instability
	Aphakia
	Anterior-chamber intraocular lens present
	Sutured posterior-chamber intraocular lens with a ruptured posterior capsule present
Non-Study Eye (unilateral participants only)	
Inclusion	IOP < 25 mmHg
	No history of open-angle glaucoma (either primary open-angle glaucoma or other cause of open-angle glaucoma; note: angle-closure glaucoma is not an exclusion criterion)
	No history of steroid-induced IOP that required IOP-lowering treatment
	No exam evidence of pseudoexfoliation
Randomization Phase	
Study Eye	
Inclusion	All 3 run-in phase visits and ranibizumab injections were completed within ±10 days of the target visit date
	Randomization visit no more than 5 weeks (35 days) from 8-week visit.
	At least 21 days since prior study injection.
	Visual acuity letter score in study eye ≤78 and ≥24 (approximate Snellen equivalent 20/32 to 20/320)
	On clinical exam, definite retinal thickening due to DME involving the center of the macula
	Central subfield (CSF) thickness (microns) on optical coherence tomography (OCT) meeting either one of the following two gender- and OCT machine-specific criteria: Zeiss Cirrus: ≥290 in women, ≥305 in men; Heidelberg Spectralis: ≥305 in women, ≥320 in men
Exclusion	History of chronic renal failure requiring dialysis or kidney transplant
	A condition that, in the opinion of the investigator, would preclude participation in the study (e.g., unstable medical status including blood pressure, cardiovascular disease, and glycemic control)
	Initiation of intensive insulin treatment (a pump or multiple daily injections) within 4 months prior to randomization or plans to do so in the next 4 months
	Participation in an investigational trial that involved treatment with any drug that has not received regulatory approval for the indication being studied within 30 days of enrollment
	Known allergy to any component of the study drugs (including povidone iodine prep)
	Blood pressure > 180/110 (systolic above 180 OR diastolic above 110)
	Myocardial infarction, other acute cardiac event requiring hospitalization, stroke, transient ischemic attack, or treatment for acute congestive heart failure within one month prior to enrollment

eTable 2. Per-Protocol Analysis of Visual Acuity and Retinal Thickness [a]

	Dexamethasone + Ranibizumab [b]	Sham Treatment + Ranibizumab [b]	Adjusted Difference: Combination-Ranibizumab (95% CI) [c]	*P* Value
No. of eyes	**59**	**63**		
Visual Acuity (Letter Score) at 24 Weeks				
Mean (SD)	67 (13.2)	66 (15.1)		
Snellen equivalent, mean	20/50	20/50		
Change from randomization visit				
Median (IQR)	+2 (-1, +8)	+4 (0, +8)		
Mean (SD)	+2.5 (9.7)	+2.9 (7.0)	-0.1 (-3.6, +3.3)	.93
Central Subfield Thickness (μm) [d] at 24 Weeks				
Median (IQR)	256 (191, 316)	284 (239, 396)		
Mean (SD)	263 (97)	335 (137)		
Change from randomization visit [e]				
Median (IQR)	-93 (-148, -55)	-42 (-105, -10)		
Mean (SD)	-110 (84)	-62 (98)	-54 (-91, -17)	.01

SD, standard deviation; IQR, interquartile range

[a] Empty cells indicate not applicable.

[b] Observed data only, including only participants who received all required injections at the completed visits without receiving any non-protocol treatments and had data at the 24-week visit.

[c] Treatment group differences and the corresponding 95% CIs and *P* Values were obtained using a linear mixed model (see detailed footnote under Table 3). No imputation for missing data was performed.

[d] Optical coherence tomography values obtained by spectral-domain OCT were converted to time-domain equivalent values for analysis and reporting as follows: −43.12 + 1.01 × Zeiss Cirrus; −72.76 + 1.03 × Spectralis. One optical coherence tomography value was missing for combination group due to low resolution.

[e] Change in OCT central subfield thickness (in microns) was truncated at 3 SD from the mean [-372, +201] (calculated using observed changes at 24 weeks combining all treatment groups), to minimize the effect of outliers. Two values were truncated in the sham group: one on the negative end, and one on the positive end.

eTable 3. Pre-Planned Subgroup Analysis of Visual Acuity and Retinal Thickness [a]

	Dexamethasone + Ranibizumab		Sham Treatment + Ranibizumab		Adjusted Difference: Combination-Ranibizumab (95% CI) [b]	*P* Value for Interaction [b]
No. of eyes	**63**		**64**			
Change in Visual Acuity (Letter Score) at 24 Weeks from Randomization Visit						
Baseline lens status						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Pseudophakic	25	+5.1 (9.7)	32	+2.0 (7.6)	+3.1 (-2.1, +8.3)	.08
Phakic	38	+1.1 (9.7)	32	+4.1 (6.4)	-3.0 (-7.7, +1.7)	
Improvement in visual acuity during run-in phase [c]						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Presence	33	+2.6 (10.6)	36	+3.6 (7.0)	-1.1 (-5.8, +3.6)	.65
Absence	30	+2.8 (9.1)	28	+2.3 (7.2)	+0.4 (-4.8, +5.5)	
Improvement in OCT central subfield thickness during run-in phase [d]						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Presence	37	+4.1 (9.9)	38	+3.0 (7.2)	+1.0 (-3.6, +5.7)	.27
Absence	26	+0.7 (9.6)	26	+3.0 (7.0)	-2.6 (-8.1, +2.9)	
Change in Central Subfield Thickness (μm) [e] **at 24 Weeks from Randomization Visit**						
Baseline lens status						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Pseudophakic	25	-111 (86)	32	-49 (96)	-78 (-131, -25)	.17
Phakic	37	-110 (86)	32	-75 (99)	-30 (-78, +17)	
Improvement in visual acuity during run-in phase [c]						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Presence	33	-124 (84)	36	-63 (116)	-68 (-118, -19)	.33
Absence	29	-95 (86)	28	-61 (68)	-36 (-90, +17)	
Improvement in OCT central subfield thickness during run-in phase [d]						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Presence	36	-132 (92)	38	-73 (114)	-74 (-121, -28)	.15
Absence	26	-80 (66)	26	-47 (65)	-25 (-80, +30)	

OCT, optical coherence tomography

[a] Observed data only, including participants who completed 24-week visit. Empty cells indicate not applicable.

[b] Treatment group differences and the corresponding 95% CIs and *P* Values were obtained from a linear mixed model mimicking the primary analysis model by adding an interaction between subgroup and treatment. No imputation for missing data was performed. See detailed footnote under Table 3.

[c] Presence or absence of improvement in visual acuity during the run-in phase, defined as five or more letter gain in visual acuity at any run-in visit, compared with the prior visit.

[d] Presence or absence of improvement in retinal thickness during the run-in phase, defined as reduction in central subfield thickness by 10% at any run-in visit, compared with the prior visit.

[e] Change in OCT central subfield thickness (in microns) was truncated at 3 SD from the mean [-372, +201], (calculated using observed changes at 24 weeks combining all treatment groups), to minimize the effect of outliers. Two values were truncated in the sham group: one on the negative end, and one on the positive end.

eTable 4. Post Hoc Subgroup Analysis of Visual Acuity [a]

	Dexamethasone + Ranibizumab		Sham Treatment + Ranibizumab		Adjusted Difference: Combination-Ranibizumab (95% CI) [c]	*P* Value for Interaction [c]
No. of eyes	**63**		**64**			
Change in Visual Acuity (Letter Score) at 24 Weeks from Randomization Visit						
Baseline visual acuity						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
Worse than 20/50 (<64)	27	+6.2 (11.6)	27	+3.3 (8.2)	+2.7 (-2.6, +8.1)	.10
20/50 or better (≥64)	36	0 (7.4)	37	+2.8 (6.3)	-3.0 (-7.5, +1.6)	
Number of anti-VEGF injections within 20 weeks prior to run-in [b]						
	No. of eyes	Mean (SD)	No. of eyes	Mean (SD)		
3 injections	32	+4.8 (9.5)	44	+3.3 (7.1)	+1.3 (-3.4, +6.0)	.25
≥ 4 injections	27	-0.2 (10.3)	19	+2.5 (7.2)	-2.8 (-8.9, +3.3)	

anti-VEGF, anti-vascular endothelial growth factor

[a] Observed data only, including participants who completed 24-week visit. Empty cells indicate not applicable.

[b] Treatment group differences and the corresponding 95% CIs and *P* Values were obtained from a linear mixed model mimicking the primary analysis by adding an interaction between subgroup and treatment. No imputation for missing data was performed. See detailed footnote under Table 3.

[c] Five participants (4 in combination and 1 in ranibizumab group) reported number of injections within 36 weeks instead and thus were excluded from the analysis.

eTable 5. Ocular Adverse Events During Randomization Phase

	Dexamethasone + Ranibizumab	Sham Treatment + Ranibizumab	*P* Value [b]
No. (%) of study eyes	**65 (100)**	**64 (100)**	
Eyes with at least one ocular adverse event [a]	41 (63)	20 (31)	<.001
Increased intraocular pressure (defined as any of the below)	19 (29)	0	<.001
Increase ≥ 10 mmHg from randomization at any visit	15 (23)	0	<.001
IOP ≥ 30 mmHg at any visit	10 (15)	0	.001
Received ocular anti-hypertensives	13 (20)	0	<.001
Endophthalmitis	0	0	
Inflammation	1 (2) [c]	0	1.00
Any retinal detachment	1 (2)	0	1.00
Traction retinal detachment	0	0	
Rhegmatogenous retinal detachment	1 (2)	0	1.00
Unspecified retinal detachment	0	0	
Retinal tears	0	0	
Retinal hemorrhage	0	0	
Vitreous hemorrhage	1 (2)	0	1.00
Cataract extractions	3 (5) [c]	0	.24
Glaucoma surgery	0	0	
Received post-injection treatment to lower IOP	9 (14)	4 (6)	.24
Migration of dexamethasone implant to the anterior chamber and subsequent corneal complications	0	N/A	

IOP, intraocular pressure

[a] Some events may have been reported more than once (i.e. at multiple visits). Including study eyes that experienced at least one adverse event of interest.

[b] *P* Value to compare treatment group difference in proportions using Fisher's exact test.

[c] One participant reported both inflammation and cataract extractions.

eTable 6. Systemic Adverse Events During Randomization Phase

	Dexamethasone + Ranibizumab	Sham Treatment + Ranibizumab	Bilateral	*P* Value [f]
No. (%) of randomized participants	**52 (100)**	**51 (100)**	**13 (100)**	
No. (%) of participants with at least one systemic adverse event [a]	25 (48)	21 (41)	7 (54)	.55
No. (%) of participants with at least one serious systemic adverse event [b]	5 (10)	7 (14)	1 (8)	.55
No. (%) of participants with at least one hospitalization	5 (10)	7 (14)	1 (8)	.55
No. (%) of death	0	0	0	
No. (%) of participants with at least one non-fatal myocardial infarction [c]	0	0	0	
No. (%) of participants with at least one non-fatal stroke (ischemic, hemorrhagic, or unknown) [c]	0	1 (2)	0	.50
No. (%) of vascular death [d]	0	0	0	
No. (%) of participants with at least one APTC cardiovascular/cerebrovascular event [e]	0	1 (2)	0	.50

[a] Some events may have been reported more than once (i.e. at multiple visits)

[b] A serious adverse event is defined as an event that meets one or more of the following criteria: results in death; is life threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect. Listing of unique serious adverse events: Combination group: abdominal pain, acute kidney injury, diastolic dysfunction, multiple fractures, and upper respiratory tract infection. Ranibizumab group: acute kidney injury, cerebrovascular accident, coronary artery bypass, hypertension, hypoglycaemia, infection, pneumonia, stent placement, and vascular graft. Bilateral group: multiple fractures.

[c] Defined as no death prior to outcome time point.

[d] From any potential vascular or unknown cause

[e] Antiplatelet Trialists' Collaboration. *BMJ*. 1994 Jan 8;308(6921):81-106.

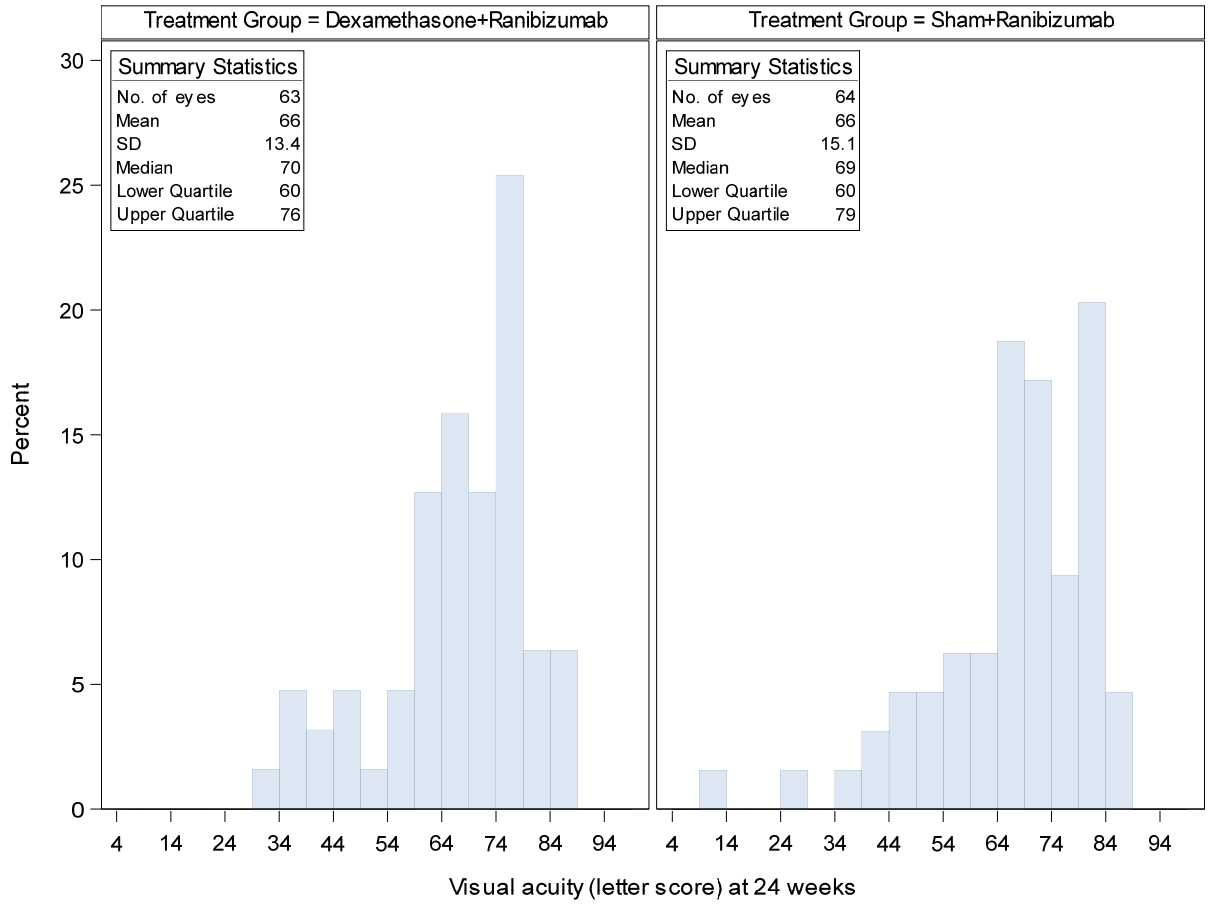
[f] *P* Value to compare treatment group difference in proportions using Fisher's exact test, including unilateral participants only.

eTable 7. All Adverse Events During Randomization Phase by MedDRA System Organ Class

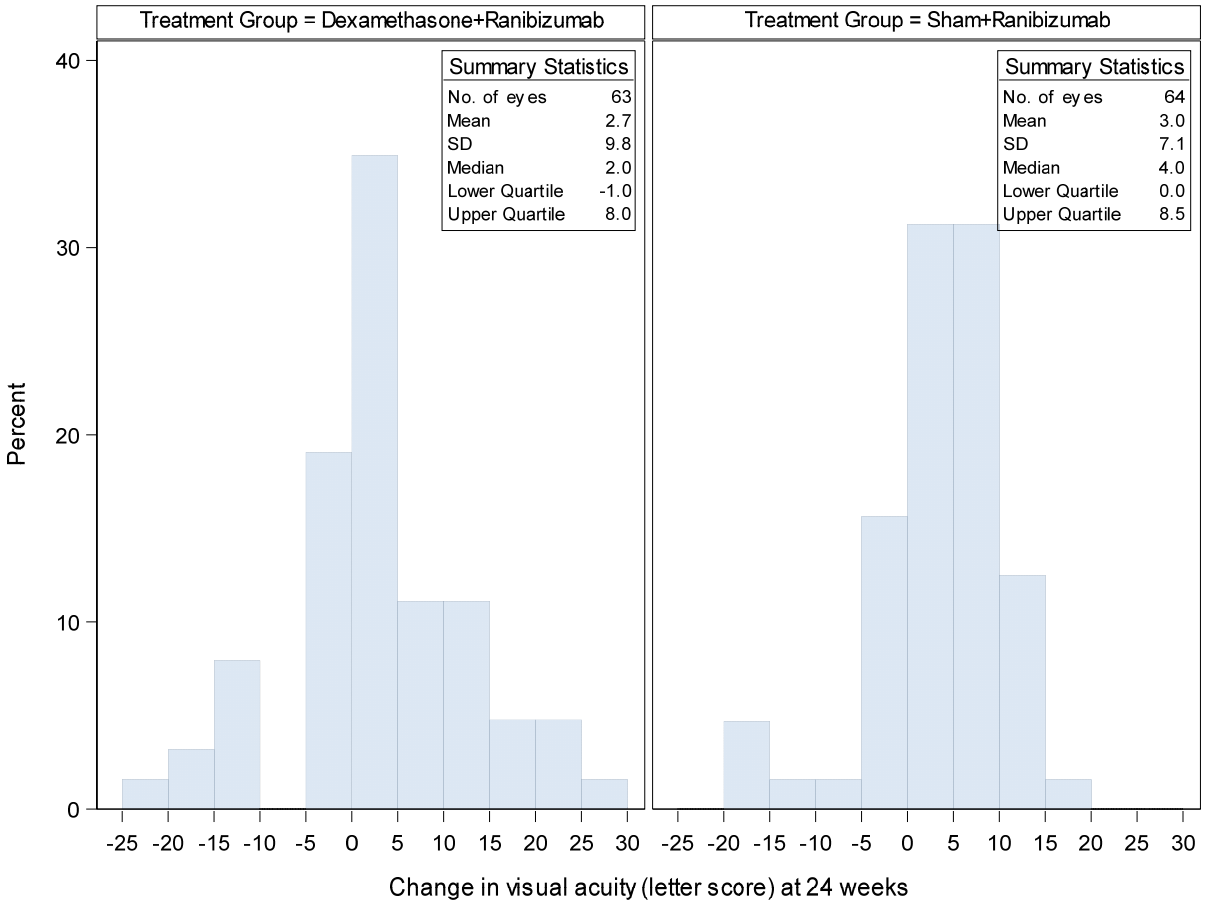
	Dexamethasone + Ranibizumab	Sham Treatment + Ranibizumab	Bilateral
No. of randomized participants	**52**	**51**	**13**
No. (%) of participants had at least one adverse event			
Blood and lymphatic system disorders	1 (2)	1 (2)	0
Cardiac disorders	2 (4)	2 (4)	0
Endocrine disorders	1 (2)	1 (2)	1 (8)
Eye disorders	26 (50)	16 (31)	2 (15)
Gastrointestinal disorders	7 (13)	3 (6)	0
General disorders and administration site conditions	0	3 (6)	0
Infections and infestations	2 (4)	6 (12)	1 (8)
Injury, poisoning and procedural complications	3 (6)	3 (6)	0
Investigations	11 (21)	1 (2)	2 (15)
Metabolism and nutrition disorders	2 (4)	1 (2)	0
Musculoskeletal and connective tissue disorders	7 (13)	5 (10)	2 (15)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2)	0	0
Nervous system disorders	2 (4)	1 (2)	1 (8)
Psychiatric disorders	0	1 (2)	1 (8)
Renal and urinary disorders	3 (6)	2 (4)	0
Respiratory, thoracic and mediastinal disorders	3 (6)	4 (8)	2 (15)
Skin and subcutaneous tissue disorders	1 (2)	0	2 (15)
Surgical and medical procedures	2 (4)	3 (6)	0
Vascular disorders	1 (2)	2 (4)	0

eFigure 1. Visual Acuity at 24 Weeks by Treatment Group Assignment

a) Visual Acuity Letter Score



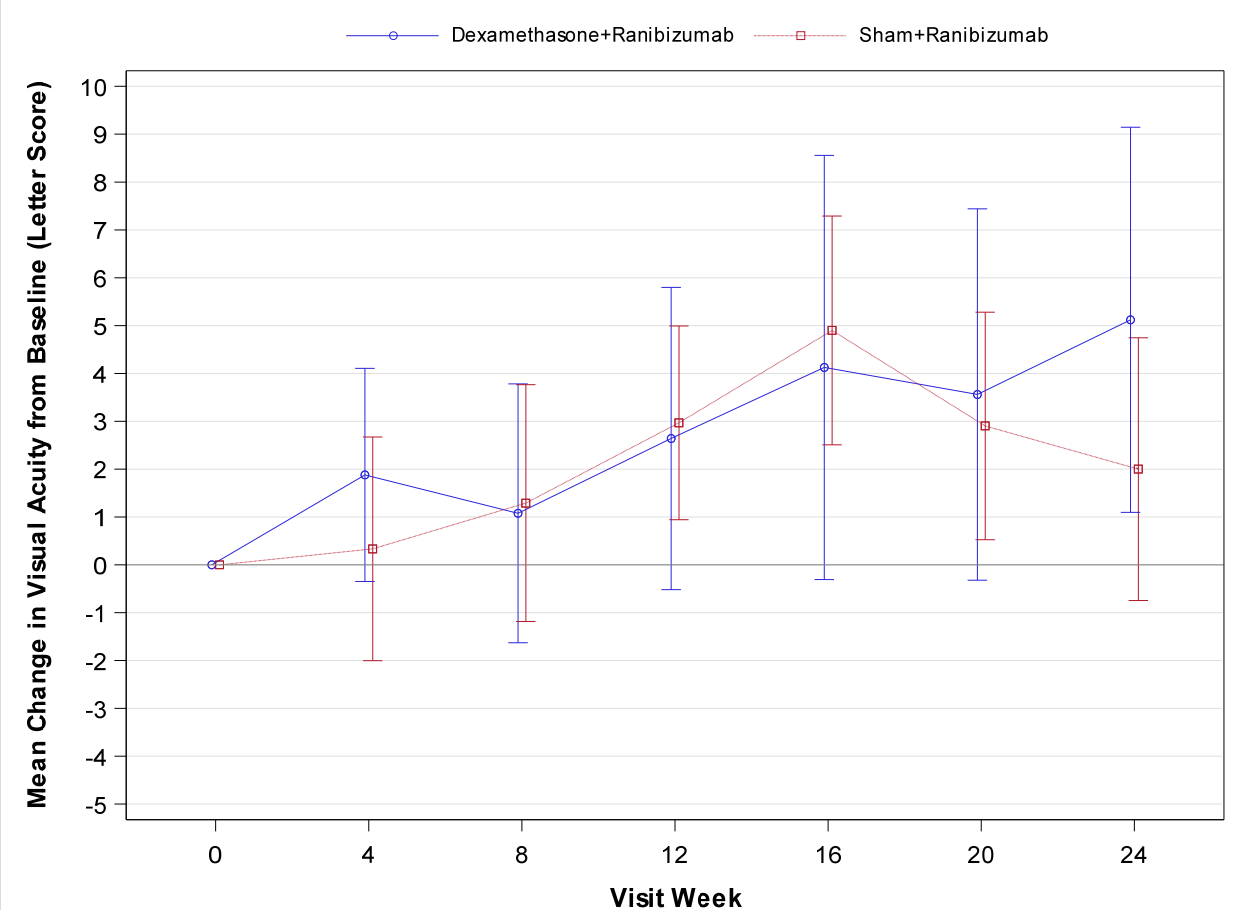
b) Change in Visual Acuity Letter Score from Randomization



Distribution of visual acuity at 24 weeks by treatment group. A) Visual acuity letter score; B) Change in visual acuity letter score from randomization visit.

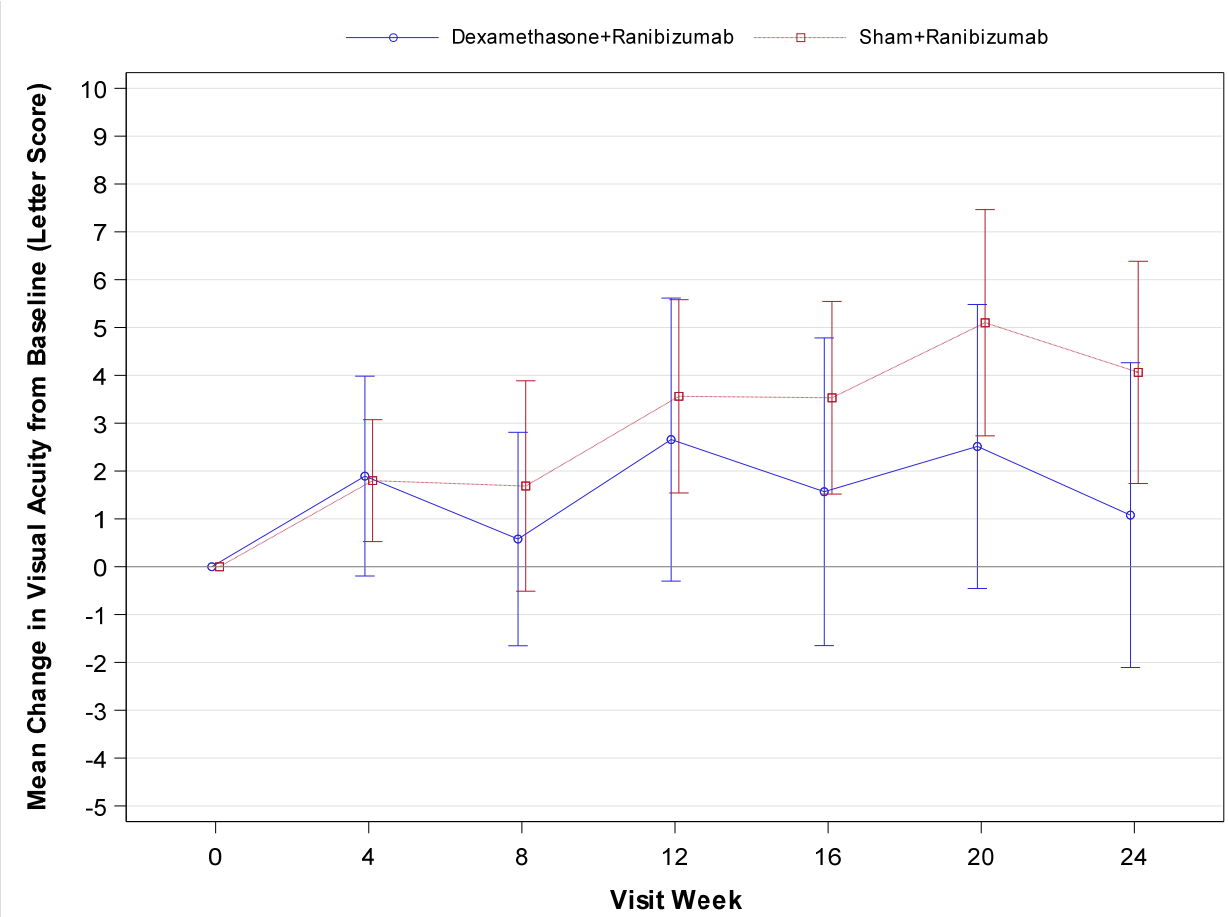
eFigure 2. Mean Change in Visual Acuity by Baseline Lens Status

a) Pseudophakic at Baseline



No. of eyes	Visit Week 0	4	8	12	16	20	24
Dexamethasone +Ranibizumab	26	25	26	25	24	25	25
Sham +Ranibizumab	32	30	31	31	30	31	32

b) Phakic at Baseline

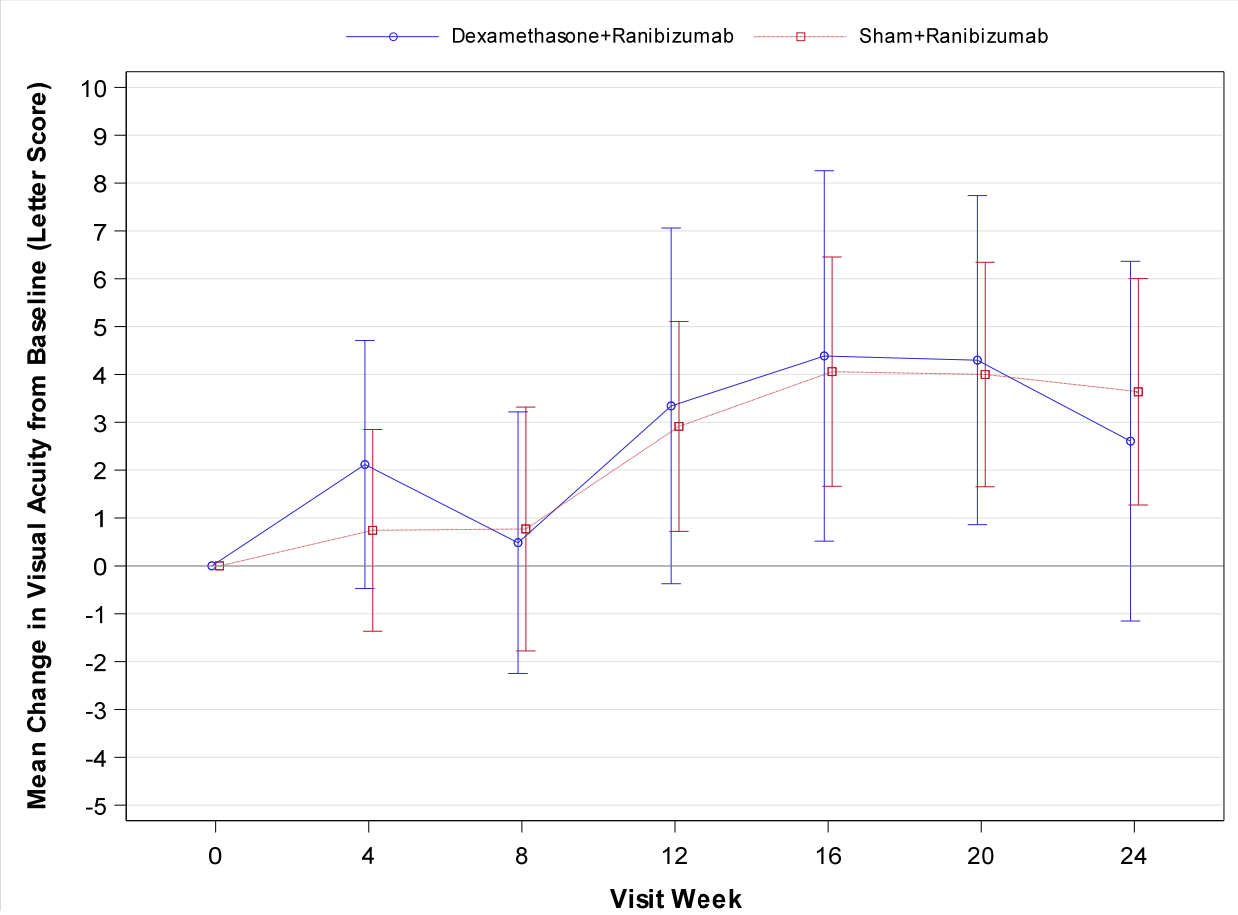


No. of eyes	Visit Week 0	4	8	12	16	20	24
Dexamethasone +Ranibizumab	39	38	38	38	37	35	38
Sham +Ranibizumab	32	30	32	32	32	30	32

Error bars indicate 95% confidence intervals. Outlying values were truncated to 3 standard deviations from the mean. A) Pseudophakic at baseline; B) Phakic at baseline. *P* = .08 for the interaction between baseline lens status and treatment.

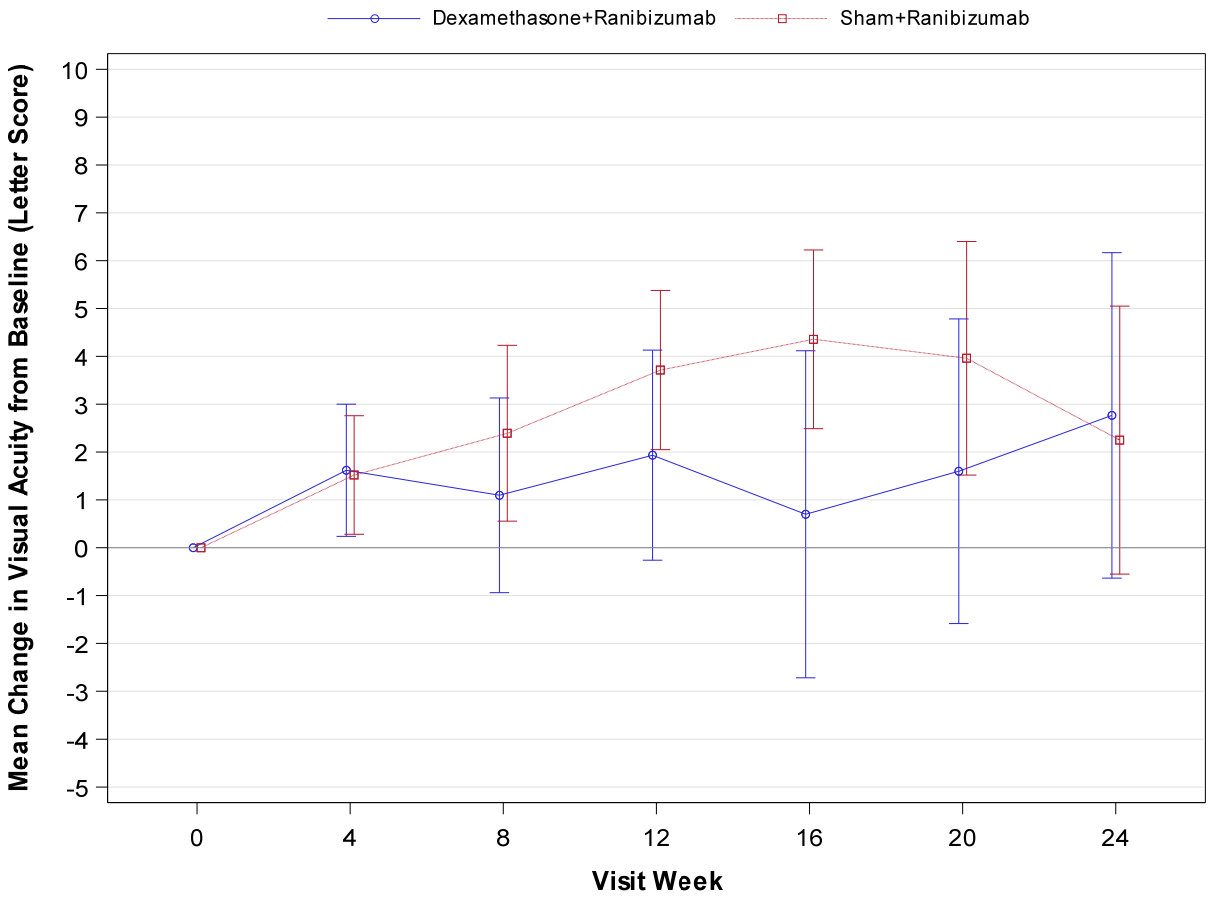
eFigure 3. Mean Change in Visual Acuity by Improvement in Visual Acuity During Run-in Phase

a) Improved



	Visit Week						
No. of eyes	**0**	**4**	**8**	**12**	**16**	**20**	**24**
Dexamethasone +Ranibizumab	34	34	33	32	31	30	33
Sham +Ranibizumab	36	35	35	35	34	35	36

b) Not Improved

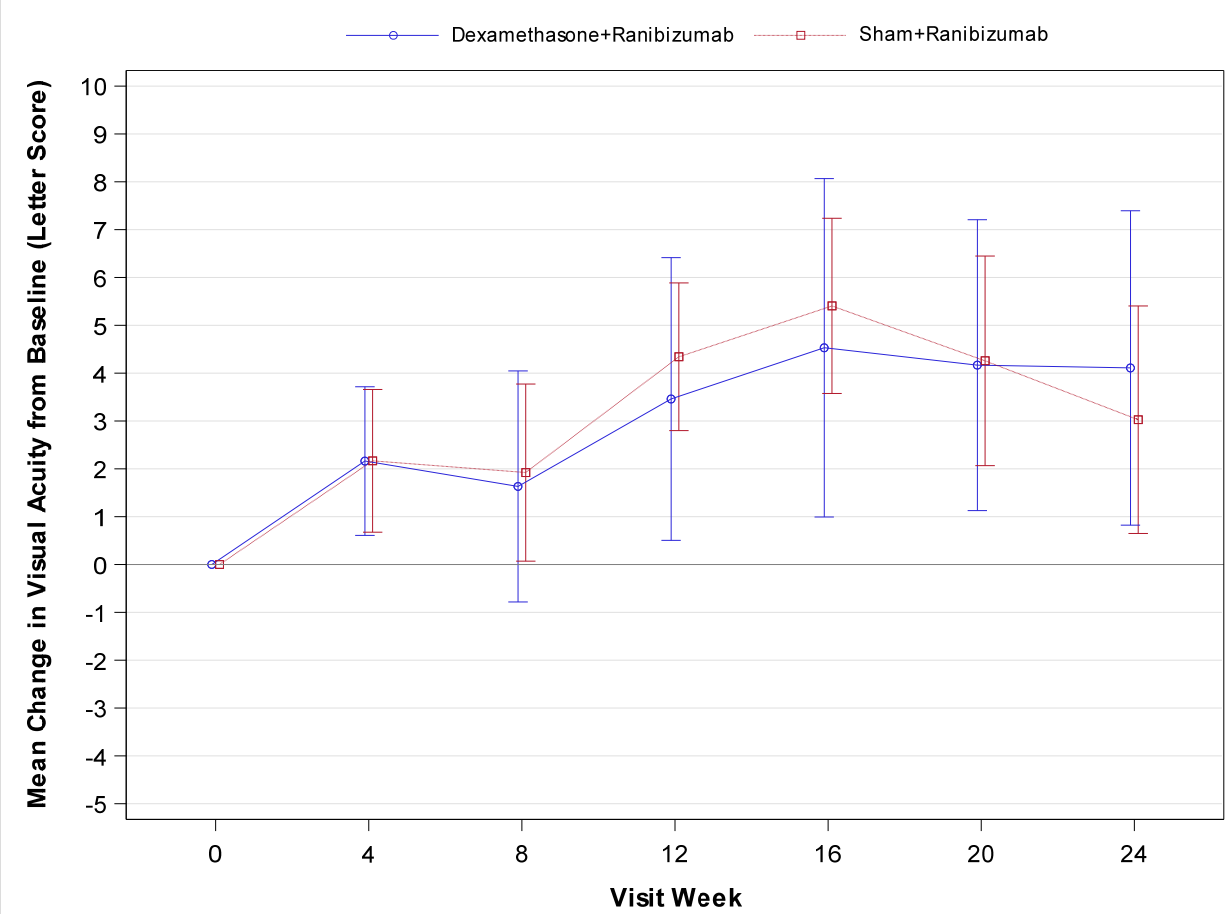


No. of eyes	Visit Week 0	4	8	12	16	20	24
Dexamethasone +Ranibizumab	31	29	31	31	30	30	30
Sham +Ranibizumab	28	25	28	28	28	26	28

Error bars indicate 95% confidence intervals. Outlying values were truncated to 3 standard deviations from the mean. A) Visual acuity improved during run-in phase; B) Visual acuity not improved during run-in phase. *P* = 0.65 for the interaction between treatment and improvement in visual acuity during run-in phase.

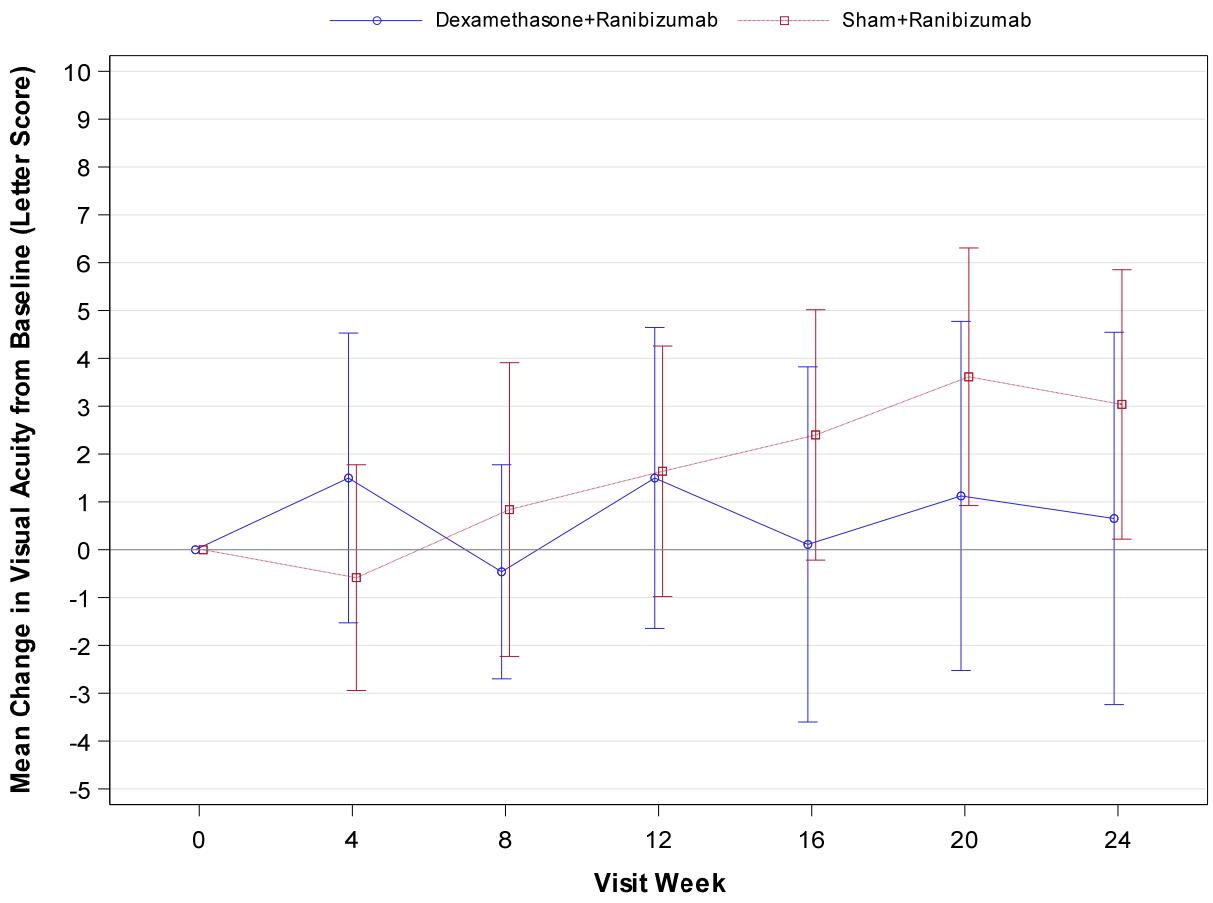
eFigure 4. Mean Change in Visual Acuity by Improvement in Central Subfield Thickness During Run-in Phase

a) Improved



	Visit Week						
No. of eyes	**0**	**4**	**8**	**12**	**16**	**20**	**24**
Dexamethasone +Ranibizumab	38	37	38	37	34	36	37
Sham +Ranibizumab	38	36	38	38	37	35	38

b) Not Improved

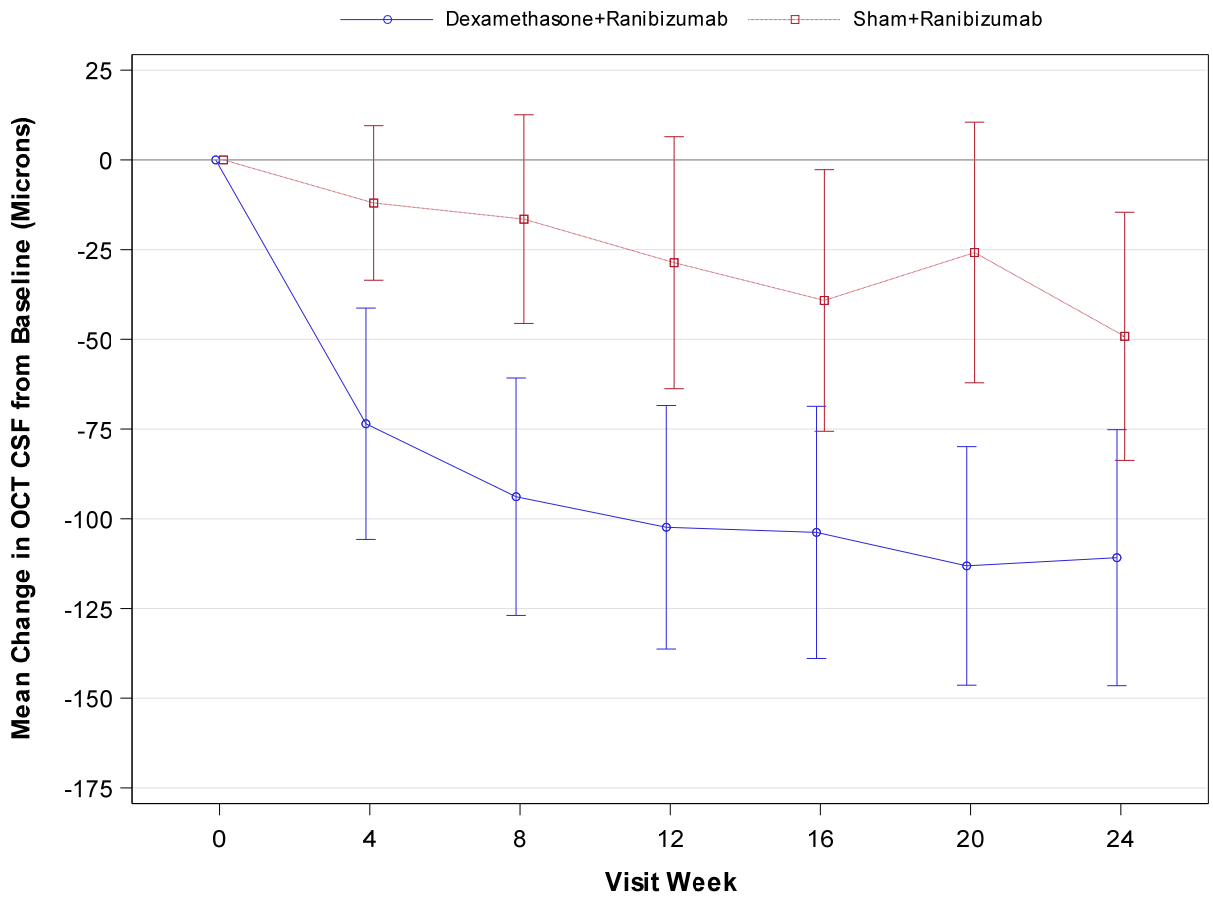


No. of eyes	Visit Week 0	4	8	12	16	20	24
Dexamethasone +Ranibizumab	27	26	26	26	27	24	26
Sham +Ranibizumab	26	24	25	25	25	26	26

Error bars indicate 95% confidence intervals. Outlying values were truncated to 3 standard deviations from the mean. A) Optical coherence tomography (OCT) central subfield thickness improved during run-in phase; B) OCT central subfield thickness not improved during run-in phase. *P* = .27 for the interaction between treatment and improvement in OCT during run-in phase.

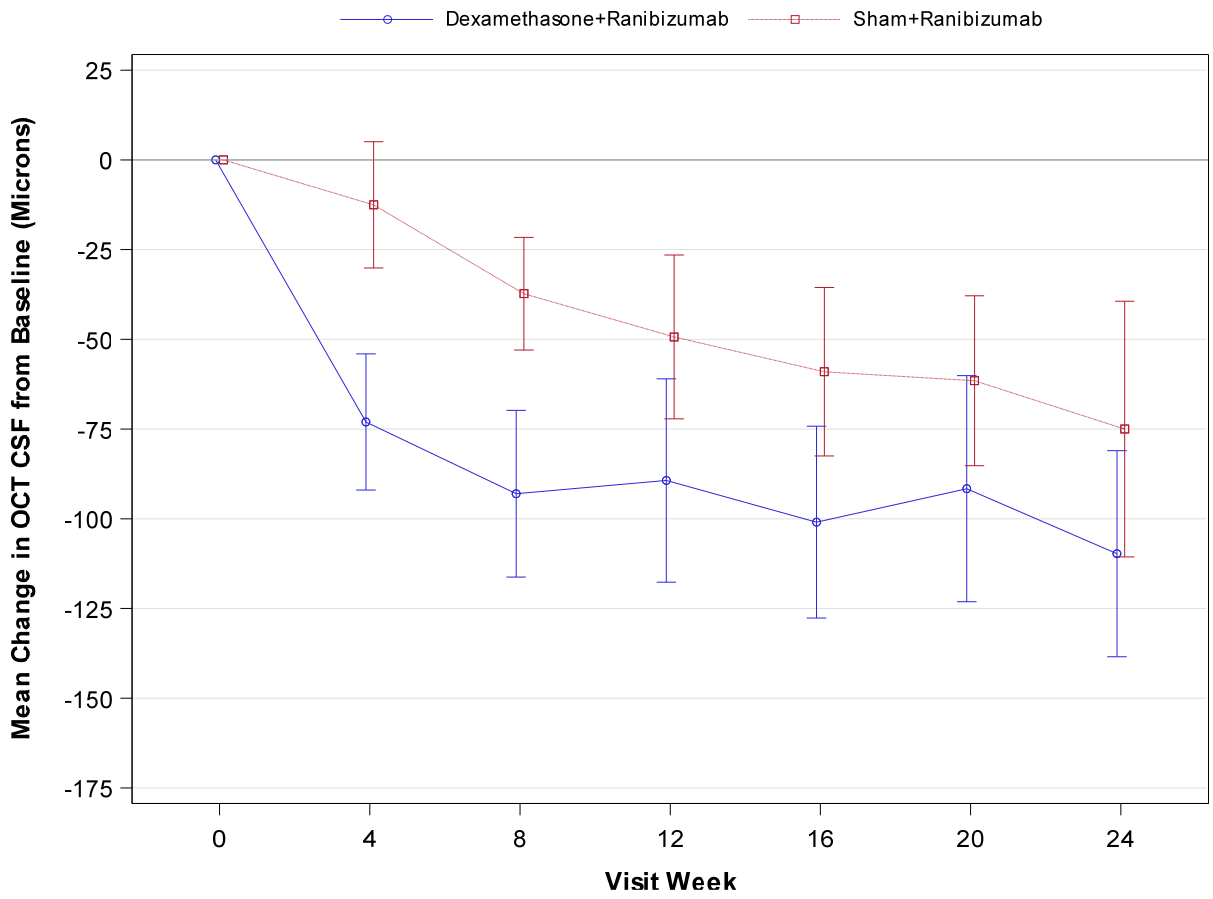
eFigure 5. Mean Change in Central Subfield Thickness by Baseline Lens Status

a) Pseudophakic at Baseline



	Visit Week						
No. of eyes	**0**	**4**	**8**	**12**	**16**	**20**	**24**
Dexamethasone +Ranibizumab	26	25	26	25	23	24	25
Sham +Ranibizumab	32	30	31	31	30	30	32

b) Phakic at Baseline



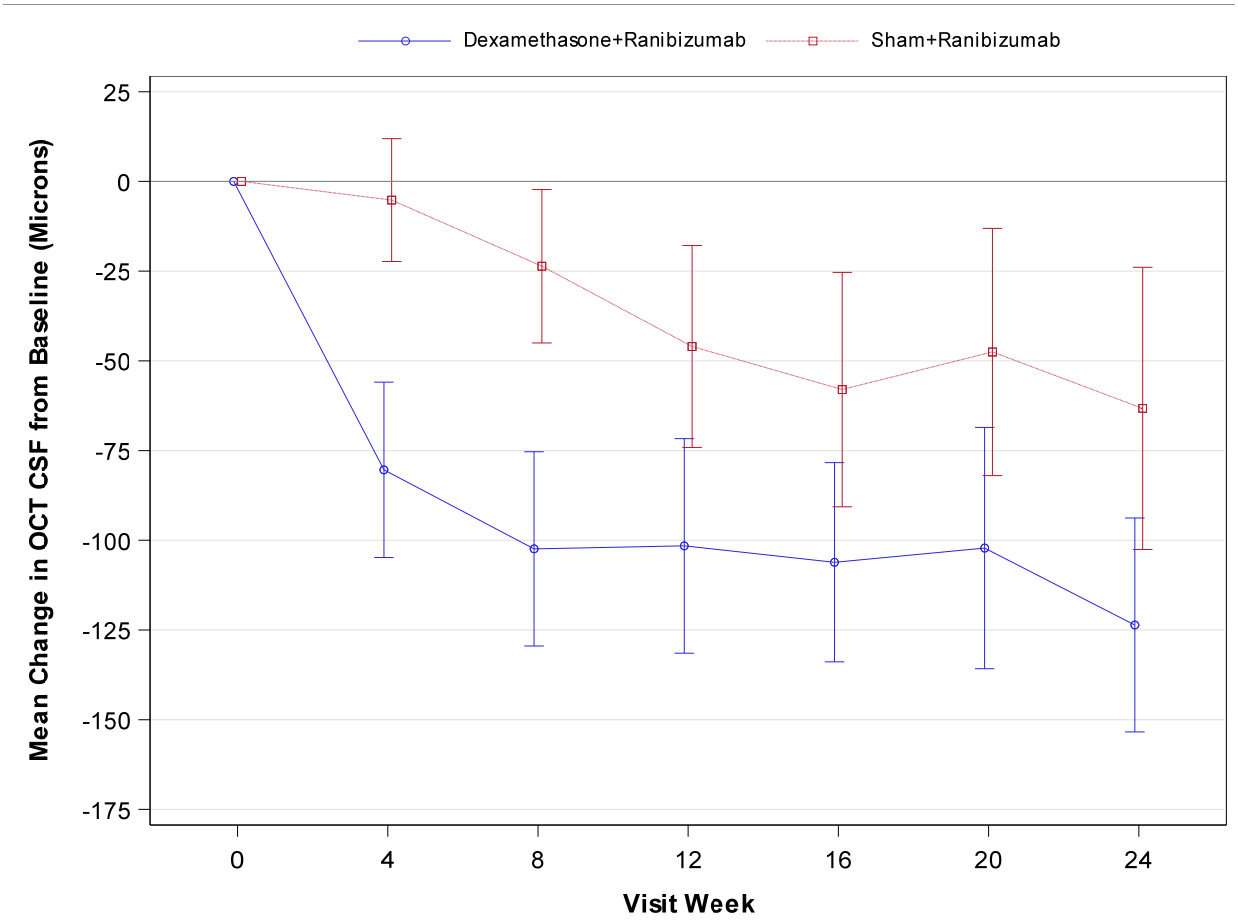
	Visit Week						
No. of eyes	**0**	**4**	**8**	**12**	**16**	**20**	**24**
Dexamethasone +Ranibizumab	39	38	38	37	37	34	37
Sham +Ranibizumab	32	30	32	32	32	30	32

OCT, optical coherence tomography; CSF, central subfield thickness

Error bars indicate 95% confidence intervals. Outlying values were truncated to 3 standard deviations from the mean. A) Pseudophakic at baseline; B) Phakic at baseline. *P* = .17 for the interaction between baseline lens status and treatment.

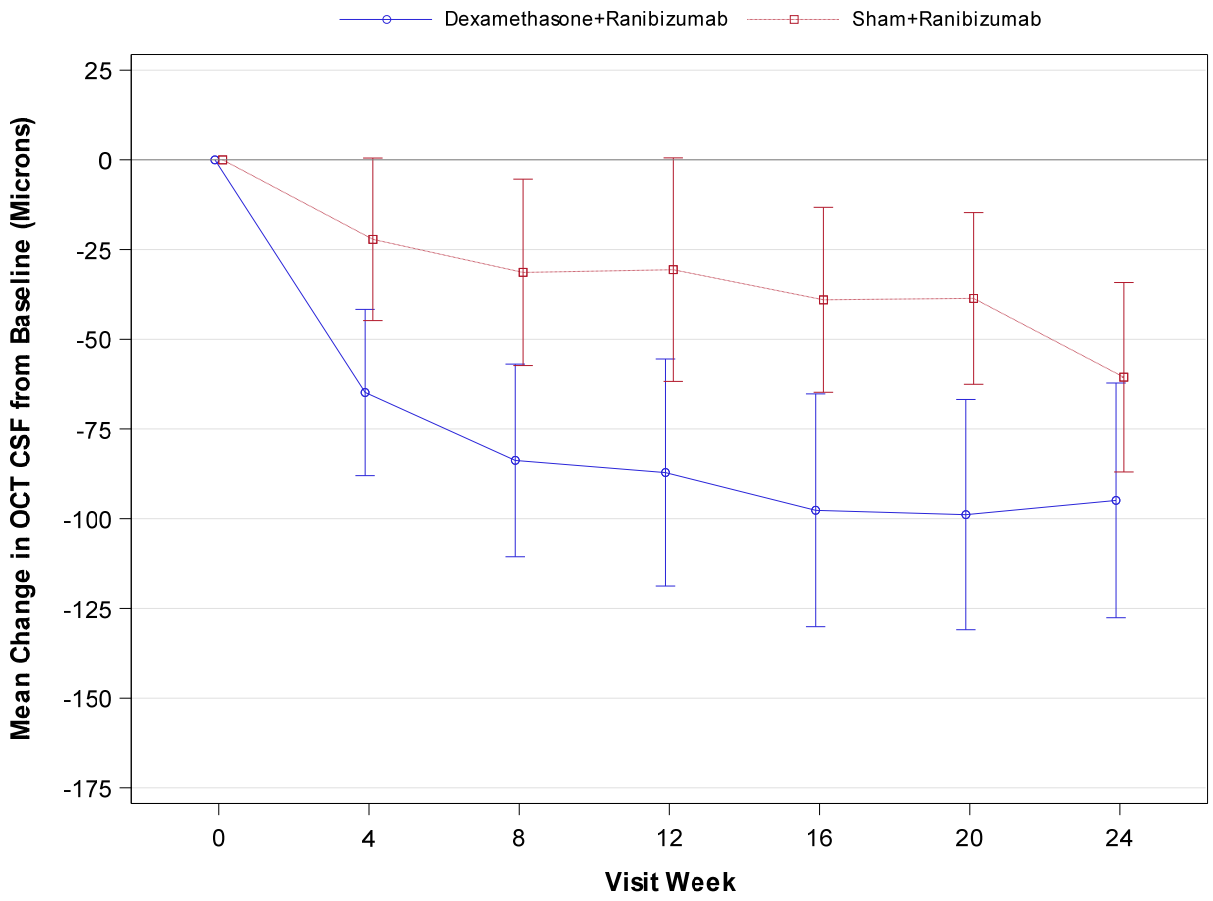
eFigure 6. Mean Change in Central Subfield Thickness by Improvement in Visual Acuity During Run-in Phase

a) Improved



No. of eyes	Visit Week 0	4	8	12	16	20	24
Dexamethasone +Ranibizumab	34	34	33	32	31	29	33
Sham +Ranibizumab	36	35	35	35	34	34	36

b) Not Improved



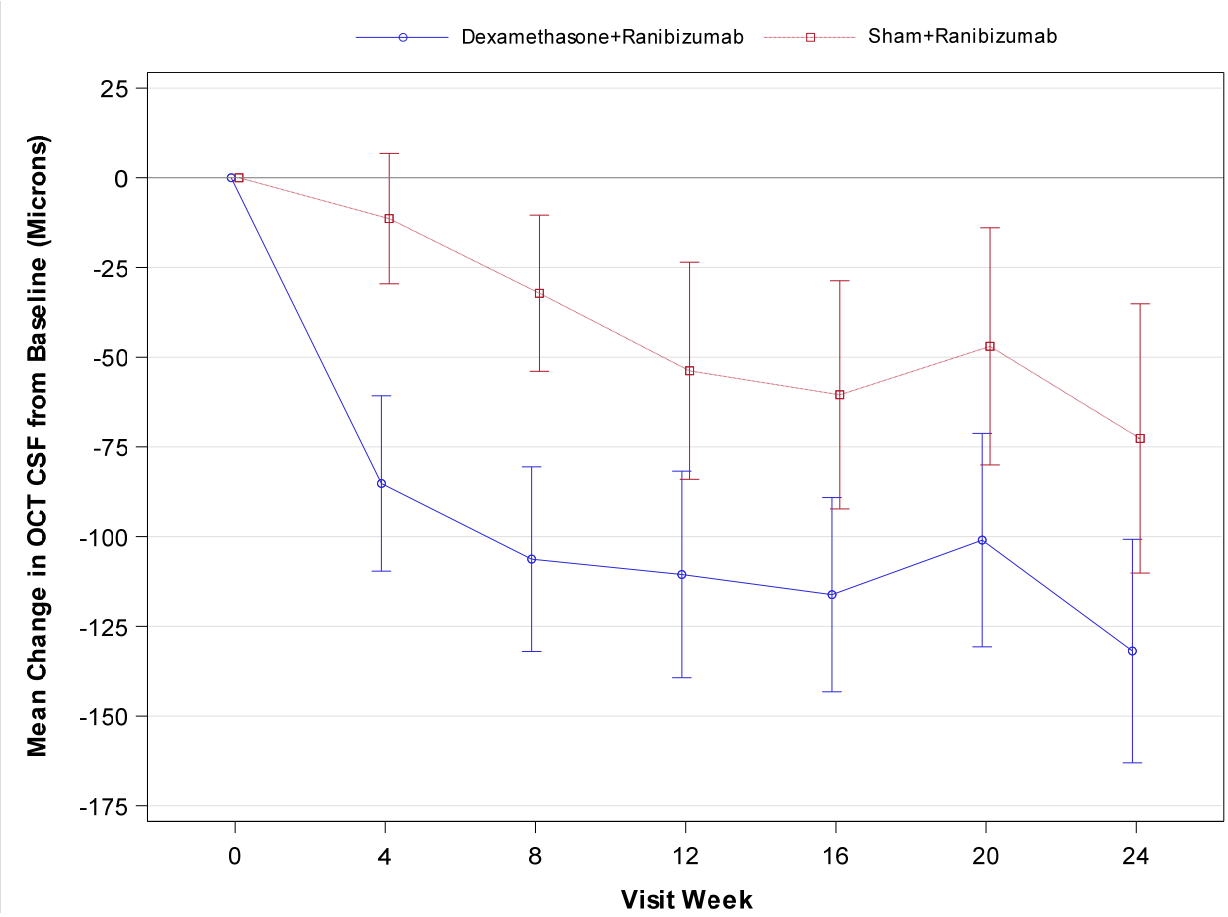
	Visit Week						
No. of eyes	**0**	**4**	**8**	**12**	**16**	**20**	**24**
Dexamethasone +Ranibizumab	31	29	31	30	29	29	29
Sham +Ranibizumab	28	25	28	28	28	26	28

OCT, optical coherence tomography; CSF, central subfield thickness

Error bars indicate 95% confidence intervals. Outlying values were truncated to 3 standard deviations from the mean. A) Visual acuity improved during run-in phase; B) Visual acuity not improved during run-in phase. *P* = .33 for the interaction between treatment and improvement in visual acuity during run-in phase.

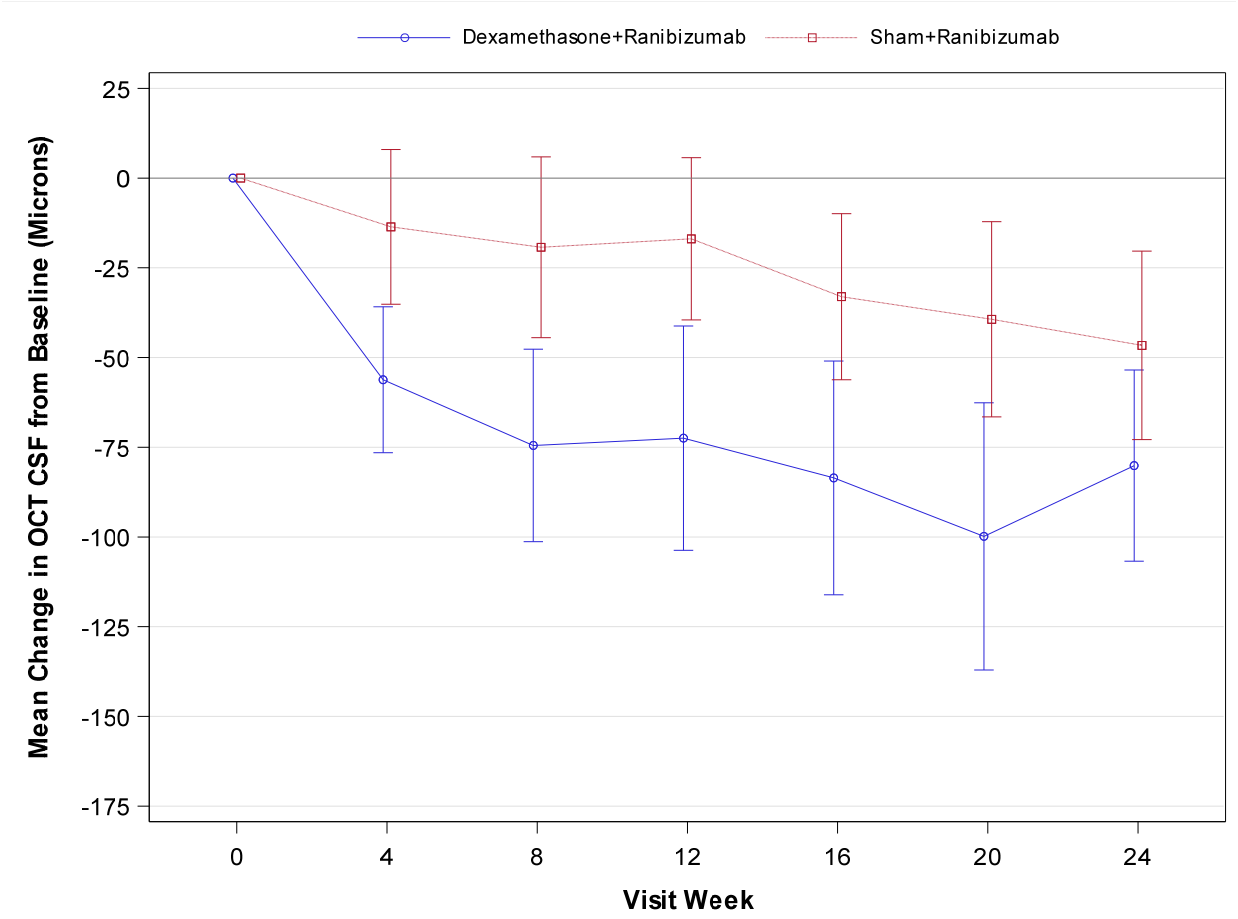
eFigure 7. Mean Change in Central Subfield Thickness by Improvement in Central Subfield Thickness During Run-in Phase

a) Improved



No. of eyes	Visit Week 0	4	8	12	16	20	24
Dexamethasone +Ranibizumab	38	36	38	36	34	35	36
Sham +Ranibizumab	38	36	38	38	37	34	38

b) Not Improved



	Visit Week						
No. of eyes	**0**	**4**	**8**	**12**	**16**	**20**	**24**
Dexamethasone +Ranibizumab	27	26	26	26	26	23	26
Sham +Ranibizumab	26	24	25	25	25	26	26

OCT, optical coherence tomography; CSF, central subfield thickness

Error bars indicate 95% confidence intervals. Outlying values were truncated to 3 standard deviations from the mean. A) OCT central subfield thickness improved during run-in phase; B) OCT central subfield thickness not improved during run-in phase. *P* = .15 for the interaction between treatment and improvement in OCT during run-in phase.

