Impact of C1q Inhibition on Visual Acuity Protection and Central Subdomain Anatomical Preservation with ANX007 in the Phase 2 ARCHER Trial

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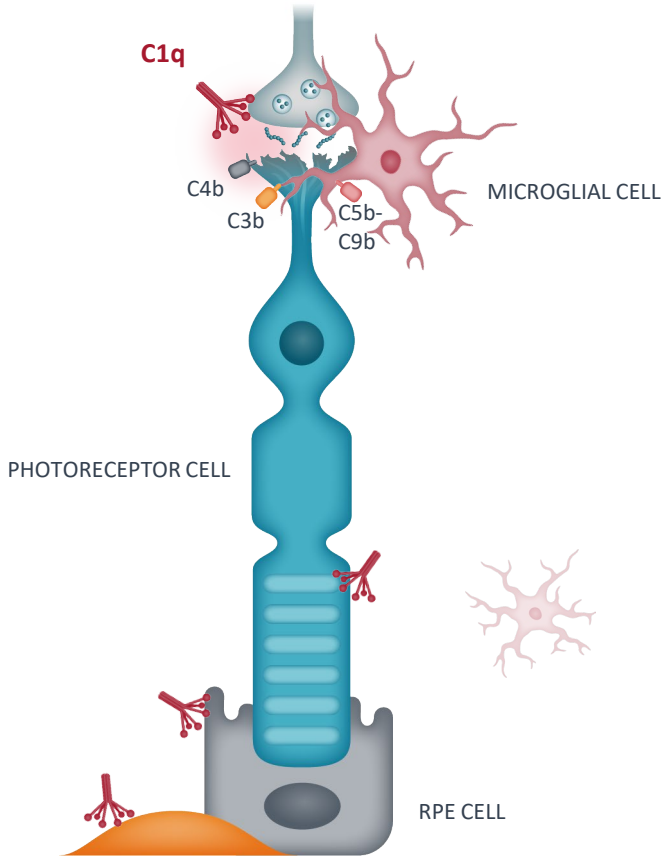
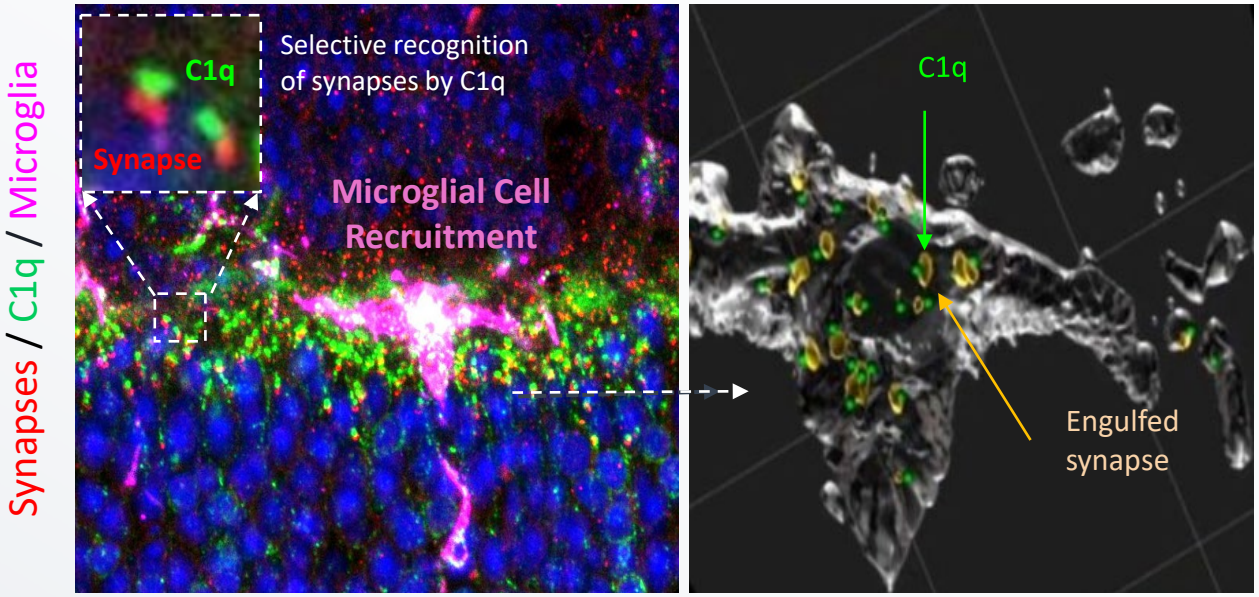
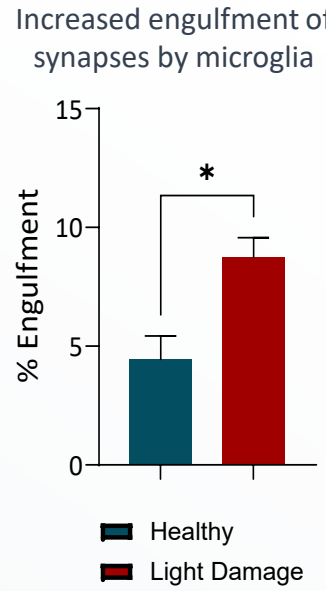
Rationale for C1q in GA: C1q Drives Synapse Destruction and Removal by Microglia in a Mouse Model of Photoreceptor Degeneration

C1q binds stressed photoreceptor synapses
and tags them for removal by microglia cells



MICROGLIAL ENGULFMENT OF C1Q-COATED SYNAPSES

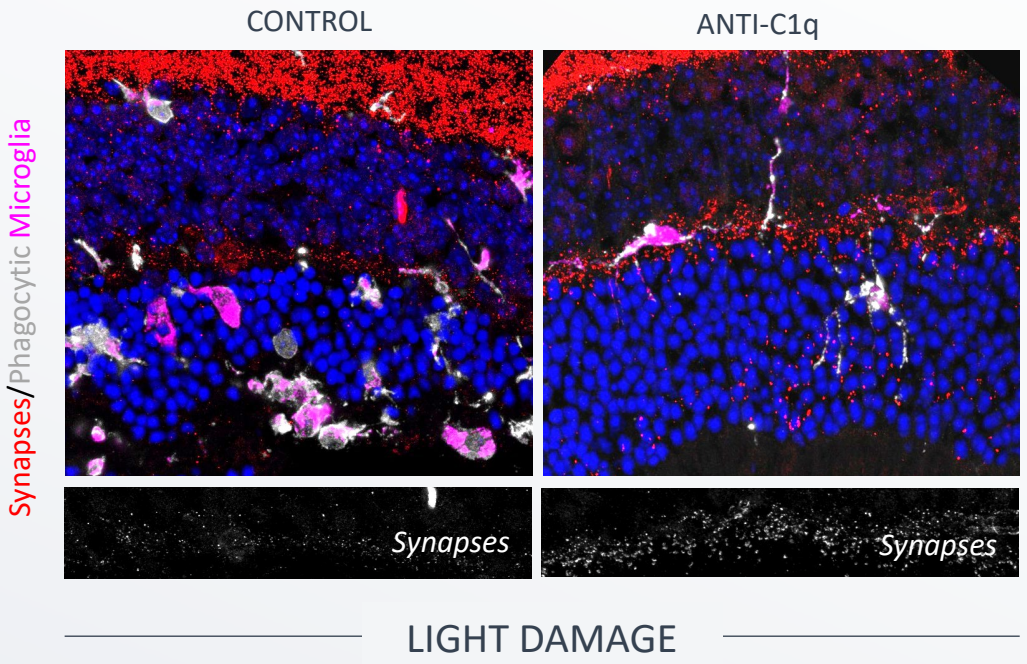




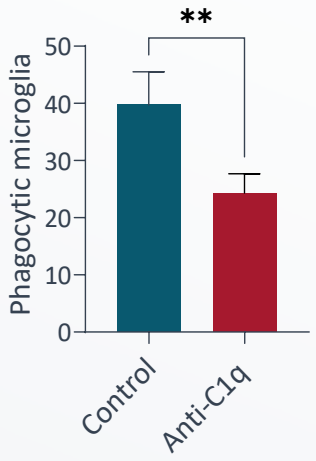
Tassoni, et al., ARVO, 2024 and Annexon on file

Rationale for C1q in GA: Anti-C1q Protected Photoreceptor Cells and Function in Mouse Models of Photoreceptor Damage

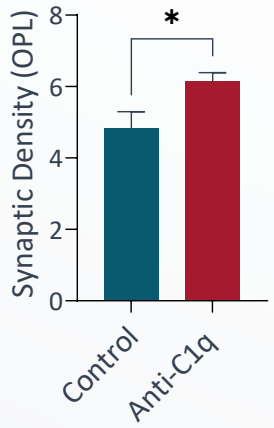
ANTI-C1Q TREATMENT REDUCED INFLAMMATION AND PRESERVED **PHOTORECEPTOR SYNAPSES AND CELL BODIES**



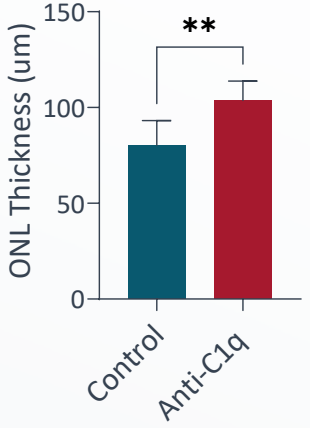
Reduced reactive **microglia**



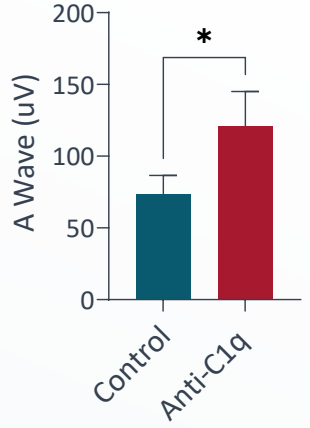
Protected photoreceptor **synapses**



Protected photoreceptor **cell bodies**



Protected retinal **function**



*p < 0.05
**p < 0.01

Tassoni, et al., ARVO 2024; Annexon data on file; Jiao, et al., 2018 *Mol Neurodegener* **13**:45;.

ANX007: Inhibitor of C1q to Treat Dry AMD and Geographic Atrophy

ANX007

IVT administered antigen-binding fragment (Fab)

KEY ATTRIBUTES

- ✓ **Design: Modeled after established IVT-administered Fab antibodies**; **same antigen recognition structure as ANX005** – full length anti-C1q antibody well tolerated as IV treatment in GBS
- ✓ **Profile:** 50kD Fab antibody; **low viscosity / non-pegylated**; <10 pM potency formulated for intravitreal administration
- ✓ **Dosing:** 5 mg / **25 µl dose in Ph3**
- ✓ **Specificity: Full target engagement** / inhibition of C1q and the classical complement pathway observed

ARCHER: Phase 2 Trial C1q Inhibitor ANX007 in Patients with Dry AMD and GA

ANX007: non-pegylated IVT-administered Fab fragment

Randomized, double-masked
Included **foveal and non-foveal** lesions
Stratified for lesion location and lesion size
12 months (n=270)

- **Sham monthly or every other month** (n=89)
- **ANX007 5mg monthly (EM)** (n=89)
- **ANX007 5mg every other month (EOM)** (n=92)

PRIMARY ENDPOINT

Rate of Change in GA lesion area as assessed by fundus autofluorescence at Month 12

PRESPECIFIED FUNCTIONAL ANALYSES

Best Corrected Visual Acuity (BCVA)
Low Luminance Visual Acuity (LLVA) & Deficit (LLVD)

Off-treatment (6 months)

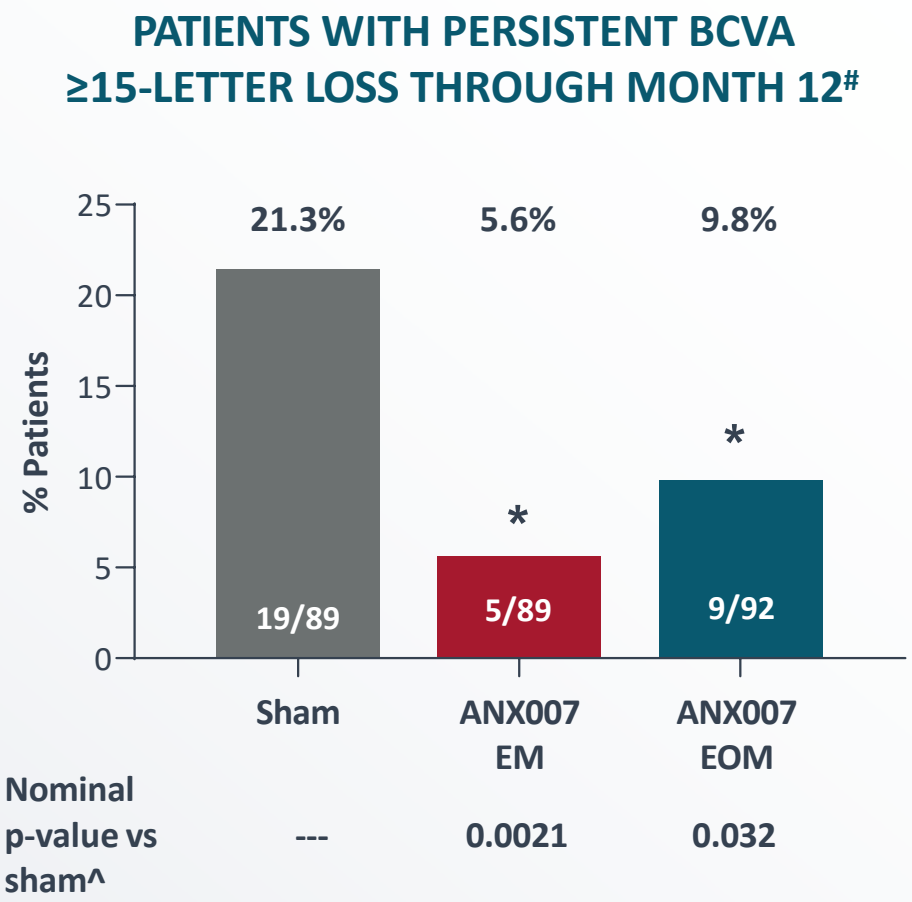
END OF STUDY
Month 18

Patient Demographics and Study Eye Baseline Characteristics Generally Well-Balanced Across Groups

CHARACTERISTIC	SHAM POOLED (N=89)	ANX007 EM (N=89)	ANX007 EOM (N=92)
Age, mean (SD)	79.8 (7.49)	79.7 (8.64)	80.5 (8.53)
Female, n (%)	59 (66.3%)	47 (52.8%)	60 (65.2%)
Caucasian, n (%)	87 (97.8%)	87 (97.8%)	89 (96.7%)
Mean BCVA, mean (SD)	**58.5 (16.2) ~20/70**	**58.8 (17.2) ~20/70**	**58.3 (15.0) ~20/70**
Foveal Lesion	49.4%	57.3%	53.3%
GA Lesion Size (mm^2), mean (SD)	7.28 (3.99)	7.28 (3.96)	7.53 (4.10)
GA Lesion < 7.5 mm^2	61.8%	58.4%	57.6%
Fellow Eye CNV	22.5%	24.7%	17.4%
Multifocality, n (%)	65 (73.0%)	61 (68.5%)	67 (72.8%)

ANX007 Demonstrated Protection From Vision Loss as Measured by BCVA ≥15-Letter Loss

A Prespecified Secondary Analysis



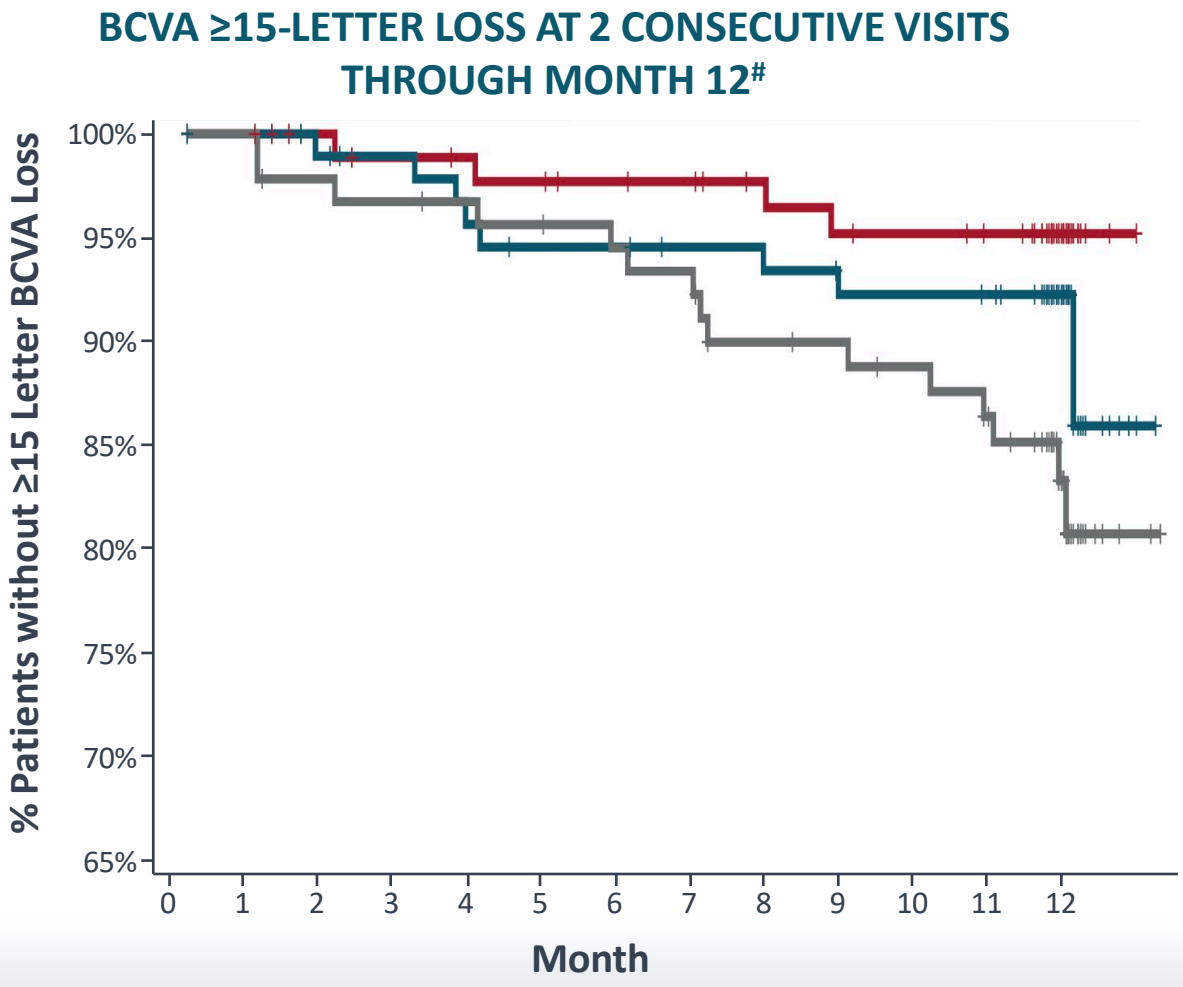
- First known clinically meaningful preservation of vision in GA
- Dose-dependent response
- BCVA ≥15-letter loss universally deemed clinically meaningful

Number Needed to Treat = 7

For every 7 patients treated with ANX007, 1 will be spared clinically significant vision loss

#Persistent for two consecutive visits through month 12 or at last study visit
^Nominal p-value from a Chi-square test in ITT population: * Nominal $p < 0.05$
Number Needed to Treat = 1 / (21.3 – 5.6) * 100= 6.4

Time-Dependent Protection From ≥15-Letter Vision Loss with ANX007 Monthly Treatment



EM (n=89)

73% Risk Reduction ANX007 EM

HR (CI) = 0.272 (0.090 to 0.819); Nominal p = 0.0098

EOM (n=92)

50% Risk Reduction ANX007 EOM

HR (CI) = 0.504 (0.214 to 1.190); Nominal p = 0.0788

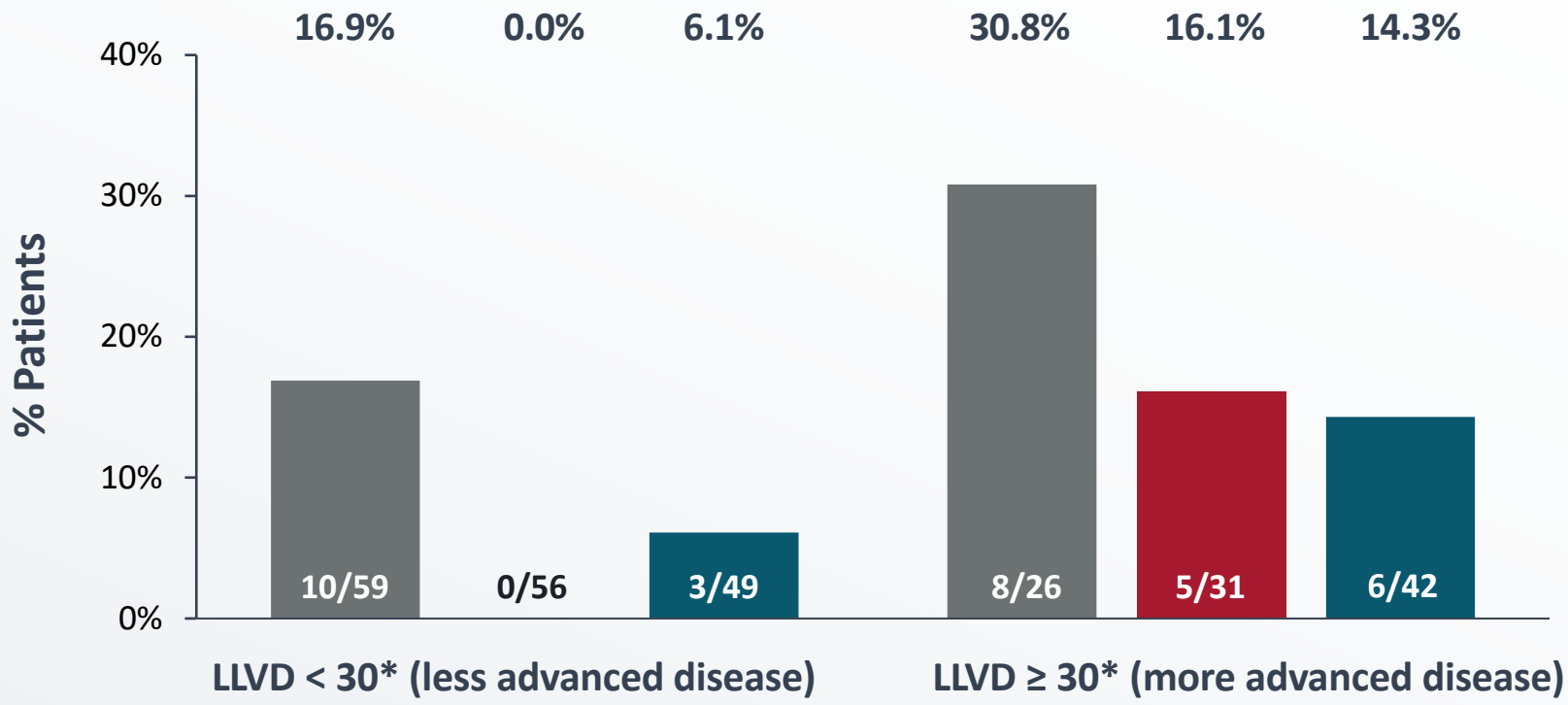
Sham (n=89)

INCREASING ANX007 IMPACT OVER TIME

HR, hazard ratio; Nominal log-rank test (versus sham) p-values are presented;
#Persistent BCVA 15-LL at two consecutive visits including month 12 supported by ensuing (off-treatment) visit
Final data

Effect of ANX007 in Eyes Relative To Low Luminance Vision Deficit at Baseline

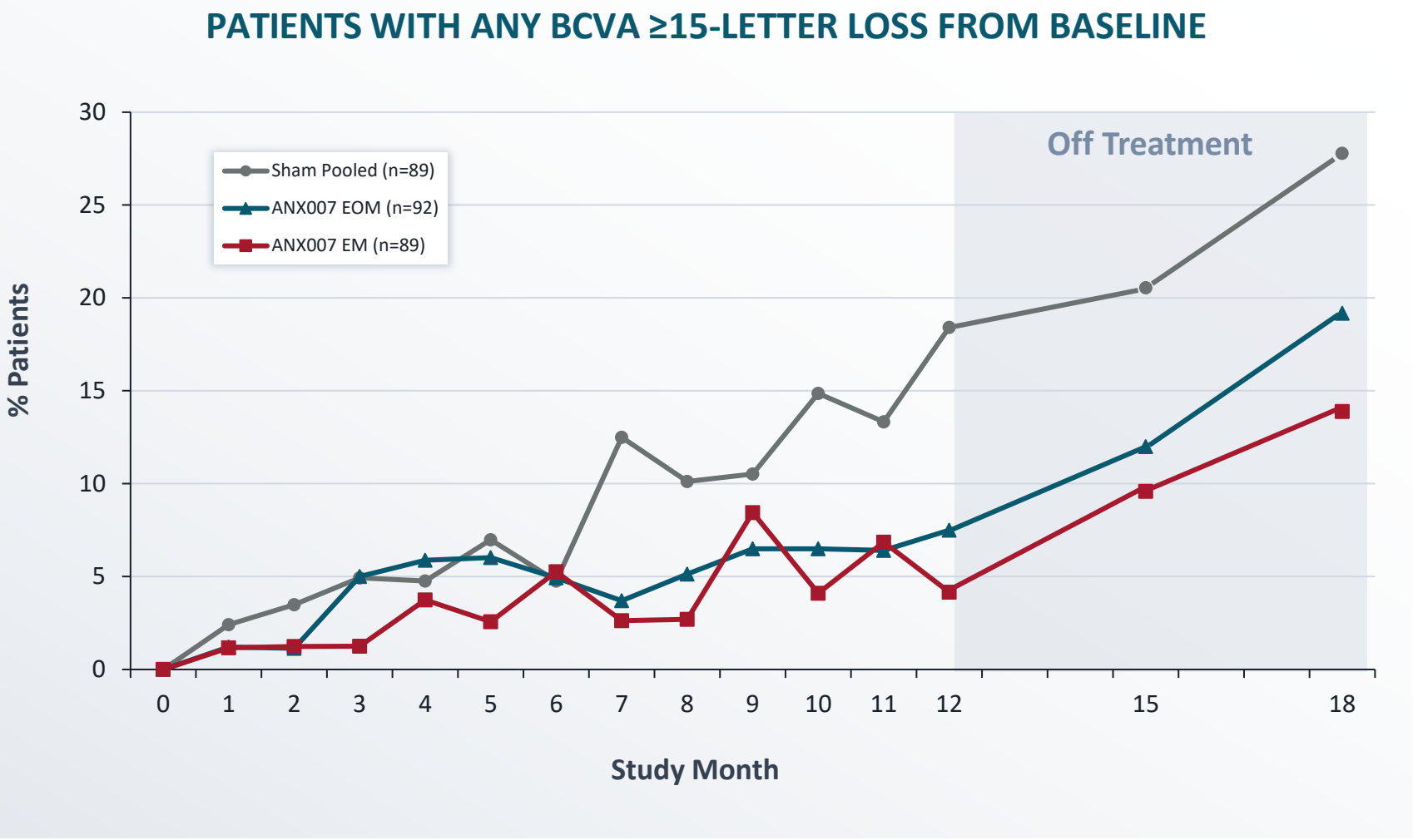
PATIENTS WITH PERSISTENT ≥15-LETTER LOSS INCLUDING MONTH 12#



Nominal summary p-value vs. sham^	
ANX007 EM (pooled)	0.0016
ANX007 EOM (pooled)	0.0183

#Persistent for two consecutive visits including month 12
^Nominal p-value from a Cochran Mantel-Haenszel test (General Association) in ITT population
*LLVD categories based on Holz FG, et al. Efficacy and Safety of Lampalizumab for Geographic Atrophy Due to Age-Related Macular Degeneration: Chroma and Spectri Phase 3 Randomized Clinical Trials. *JAMA Ophthalmol.* 2018;136(6):666–677.

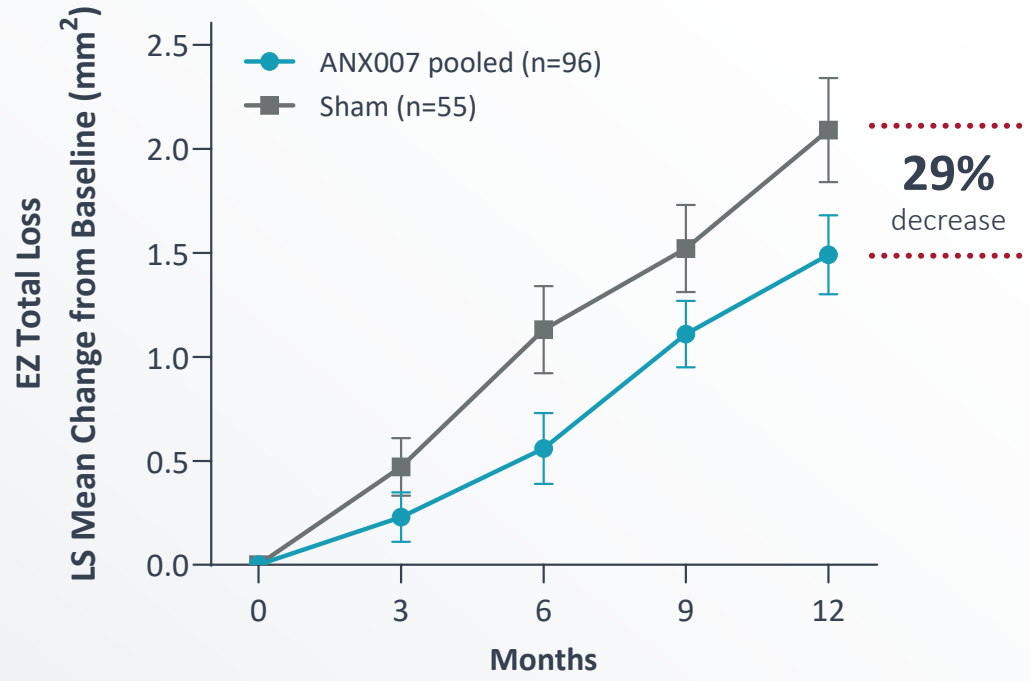
Proportion of patients with BCVA ≥15-Letter Loss Accelerated After Cessation of Treatment



- Low frequency (<0.6% per month) of single BCVA ≥15-letter losses in EM- and EOM-treated groups during 12-month treatment period
- While benefit was maintained after treatment cessation the rate of BCVA≥15 LL increased to parallel that of sham (>1.6% per month)

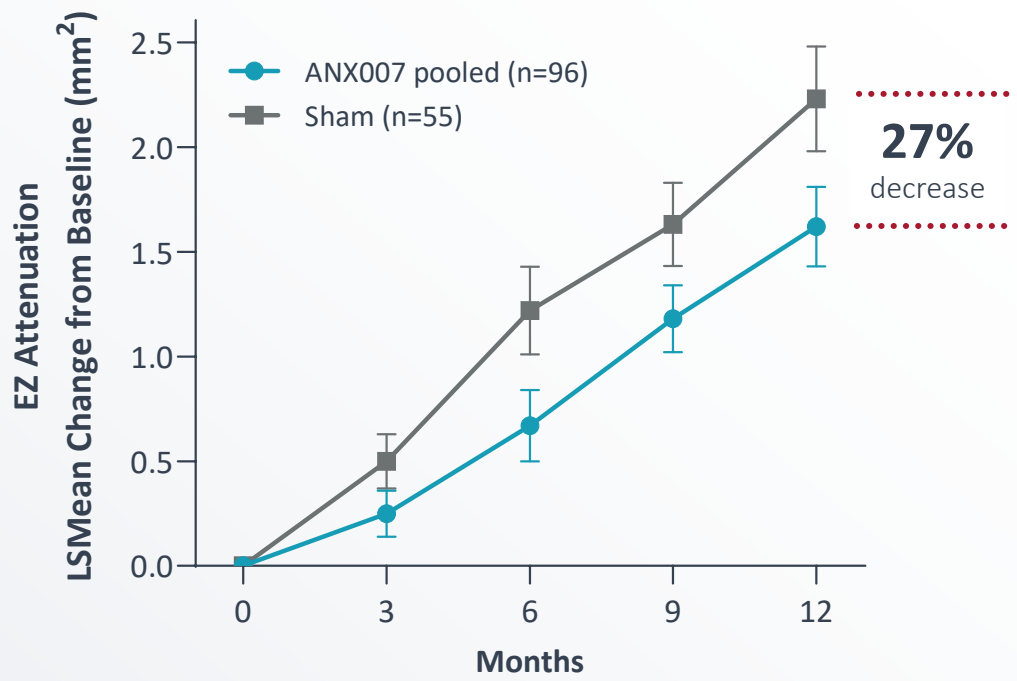
Area of EZ Loss and Attenuation was Reduced with ANX007 Through 12 Months

EZ TOTAL LOSS (EZ = 0 µm thickness)*



Nominal p-value vs sham^ ANX007 0.017

EZ ATTENUATION (EZ < 20 µm thickness)*

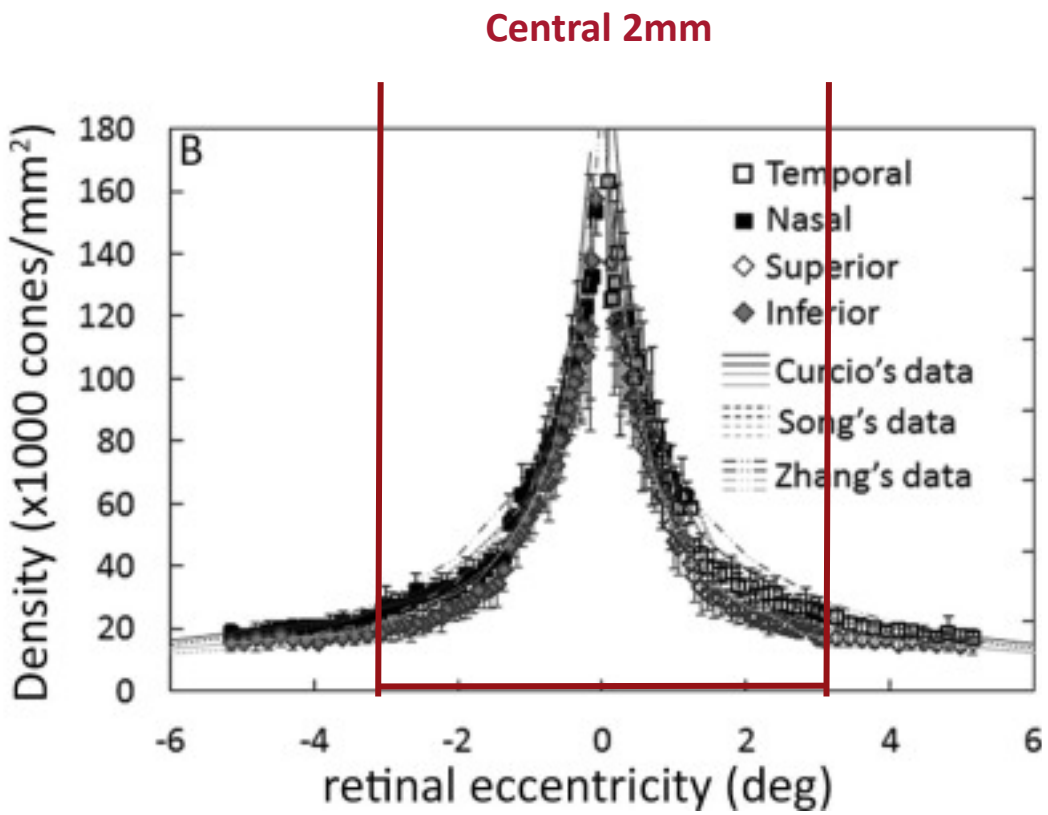


Nominal p-value vs sham^ ANX007 0.021

^Nominal p-values from a mixed model for repeated measures (MMRM) analysis; Heidelberg Spectralis OCT population with baseline OCT data (n=151)
*Two treatment groups (EM and EOM) were not different statistically

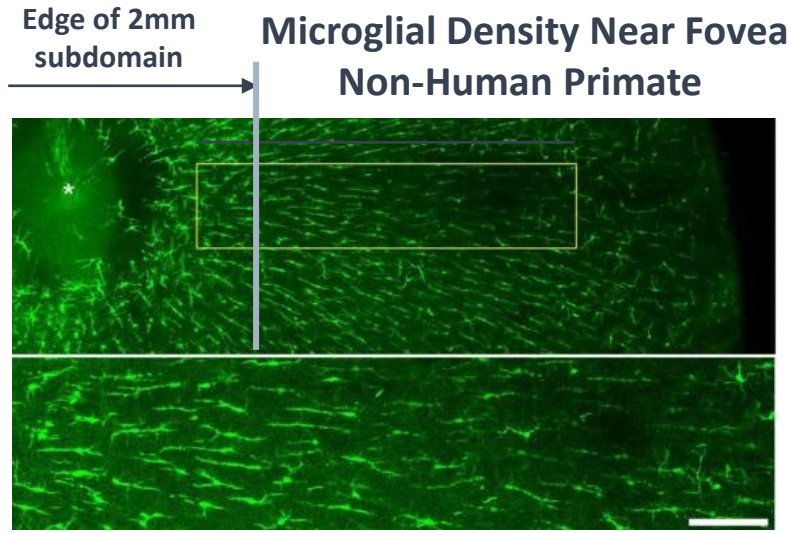
Cone and Microglia Densities Peak at the Fovea

Average Cone Density Across Retina Greatest With Central 2mm Subdomain



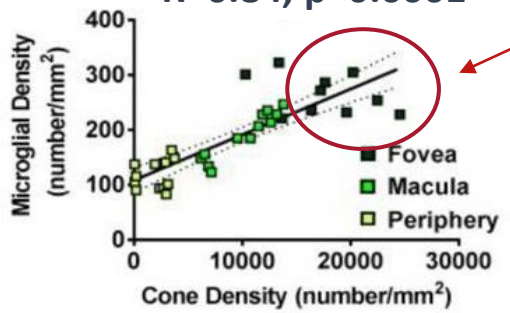
Sawides et al Vision Research, Volume 132, March 2017, Pg 34-44

Density of Microglia, C1q Effector Cell, Higher Near Central 2mm Subdomain



Correlation to Microglial Density in OPL

R=0.84, p<0.0001

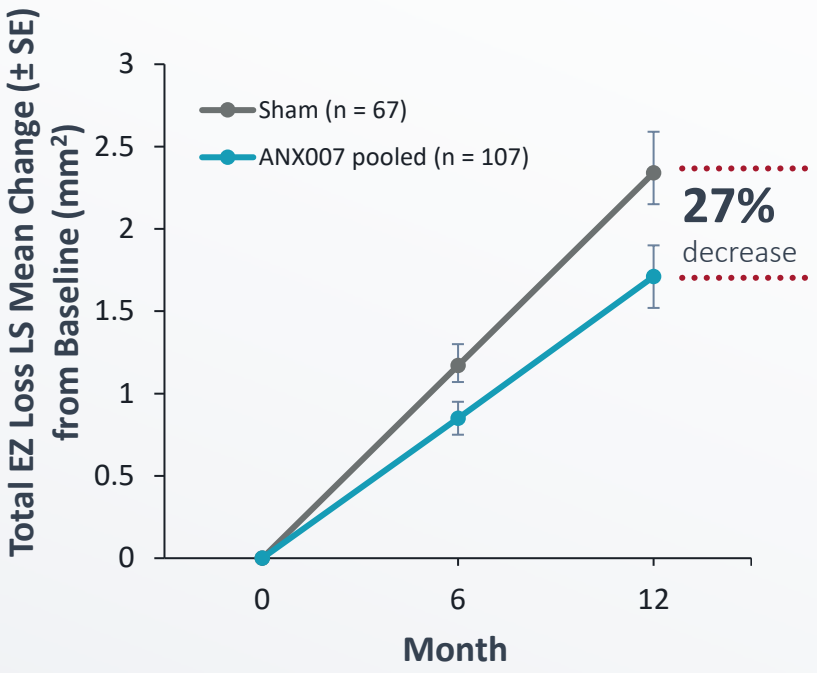


Increased cones density associated to increased microglia in OPL

Sinagravelu J, eta al. Brain Struct Funct. 2017

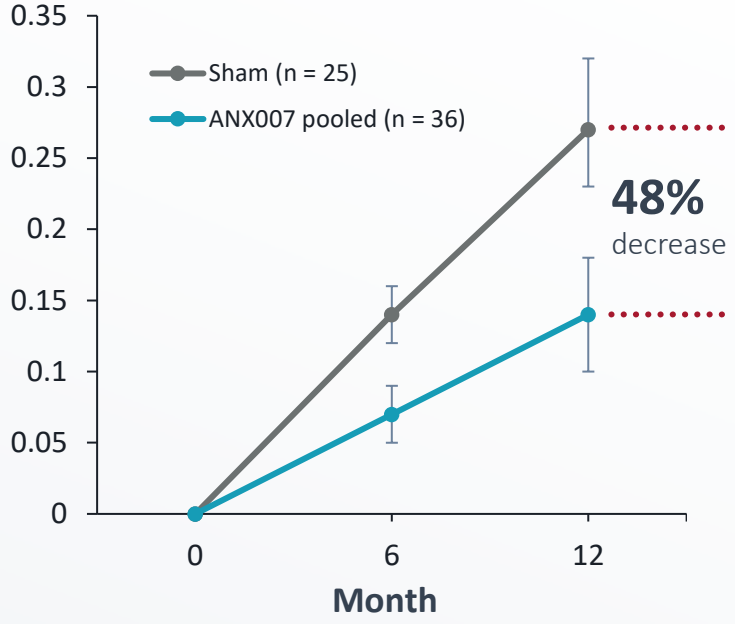
Treatment Effect with ANX007 In Reducing Total EZ Loss Area was Greater in Central 1.5 & 2 mm Through 12 Months

PAN-MACULA



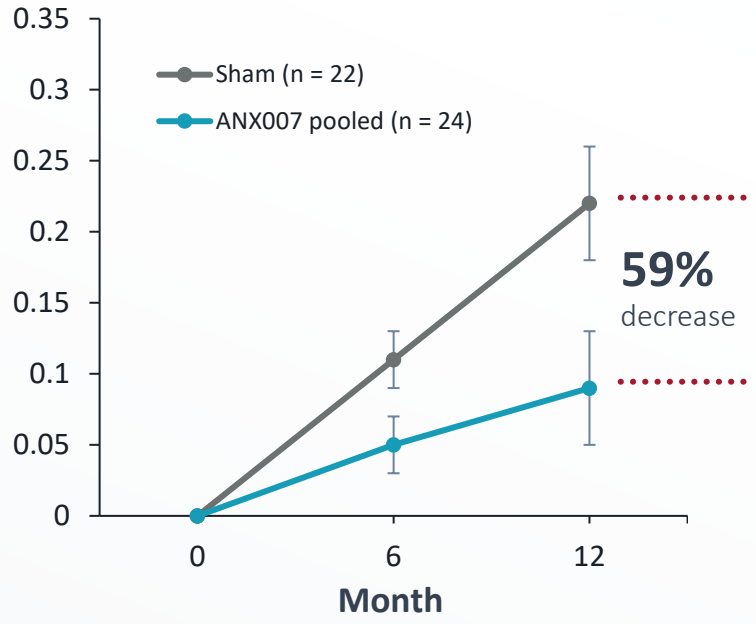
Nominal p-value^ ANX007 Pooled vs Sham 0.0457

CENTRAL 2.0 MM



ANX007 Pooled vs Sham 0.0218

CENTRAL 1.5 MM



ANX007 Pooled vs Sham 0.0319

^Nominal p-values from a linear mixed model for repeated measures model (slope) analysis;
Heidelberg Spectralis OCT population with baseline OCT data, excludes patients with >98% atrophy/attenuation at baseline

ANX007 Generally Well-Tolerated

ADVERSE EVENTS OF SPECIAL INTEREST n (%)	SHAM (N=89)	ANX007 EM (N=89)	ANX007 EOM (N=92)
Choroidal Neovascularization	3 (3.4%)	4 (4.5%)	4 (4.3%)
Endophthalmitis	0	1 (1.1%)	2 (2.2%)
Retinal Vascular Occlusion	0	0	1^ (1.1%)
Retinal Vasculitis	0	0	0
Intraocular Inflammation+	0	2 (2.2%)	1 (1.1%)
Ischemic Optic Neuropathy+	0	0	0

^Isolated cilioretinal artery occlusion; no vasculitis confirmed by DSMC and reading center
+Not AESI, included because of current interest

INTRAOCULAR INFLAMMATION DETAILS* n

Iritis – 1
Resolved with topical steroids in 2 days
No Vasculitis

Vitritis – 1
Resolved with topical steroids in 9 days
No Vasculitis

Vitreous Debris – 1
KP on endothelium, prior treatment with topical steroids
No Vasculitis

*Event Verbatim term listed

Conclusions: ANX007 Protection of Visual Function in ARCHER

- ANX007 treatment demonstrated **consistent, meaningful, dose-dependent protection of visual function** in GA patients
  - **Risk of BCVA 15-letter loss reduced by 73%** over 12 months with ANX007 EM vs sham
  - Similar, **protection** from vision loss seen **across multiple measures of visual acuity**, including significant slowing of loss of LLVA
  - On-drug preservation of vision supported by **return of visual function loss when ANX007 was discontinued**

- **Treatment Effect** with ANX007 In Reducing Total EZ Loss Area was **Greater in Central 1.5 & 2 mm** vs. pan-macula, and was **more pronounced in eyes with less EZ loss at baseline**

- **ANX007** treatment was **generally well-tolerated**; no CNV increase; no reported cases of vasculitis or ION