Visual Function Outcomes in the Phase 2 ARCHER Trial of ANX007, a C1q Inhibitor, in Participants with dry AMD with GA: Number Needed to Treat Analysis

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*A full list of ARCHER investigators can be found at https://clinicaltrials.gov/study/NCT04656561

Disclosures

Dr. Vakharia:

- **Consultant/ Advisor:** Annexon, Abbvie, Aliph, ANI Pharmaceuticals, Apellis, Astellas, Bayer, Bausch and Lomb, Coherus, Eyepoint, Genentech/Roche, Heidelberg, Notal Vision, Novartis, Ocuphire, Regeneron

- **Grant Support:** 4DMT, Alcon, Alexion, Allgenesis, Aviceda, Eyebiotech Limited, Ionis, Janssen, Kodiak, Kirwin, Kyoto, Kyowo Kirin, Ocular Therapeutics, Ocuterra, Ophthea, ONL Therapeutics, Pfizer, Priovant Therapeutics, Recens Medical, RegenxBio, Stealth Biotherapeutics, Unity, Annexon, Astellas, Bayer, Eyepoint, Genentech/Roche, Notal Vision, Novartis, Regeneron

- **Speaker:** Apellis, Astellas, Regeneron, Genentech, Bausch and Lomb

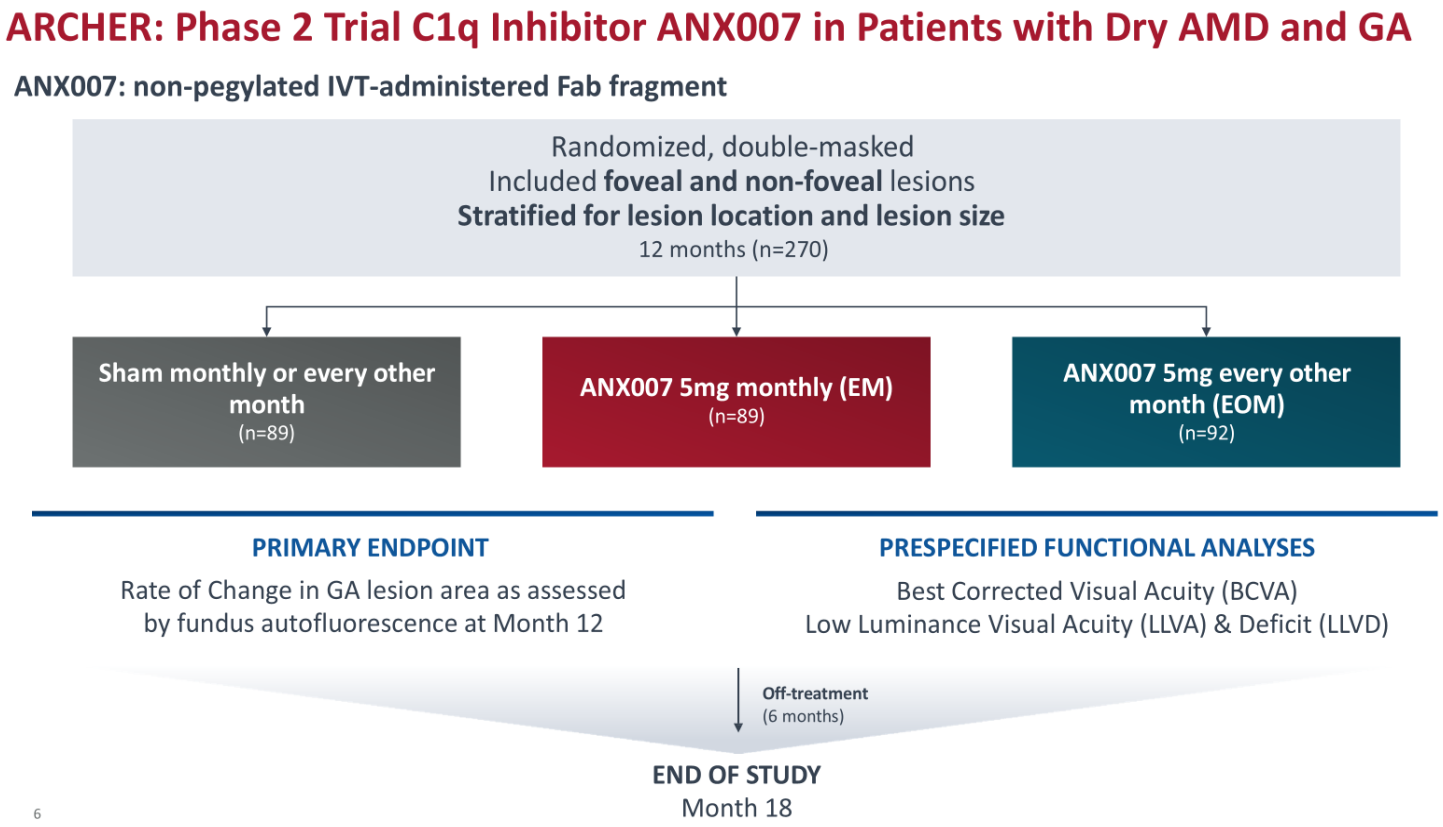
Purpose

- To report visual outcomes in the ARCHER trial in participants treated with ANX007 compared with sham treatment by considering the Number Needed to Treat (NNT).

- NNT is a calculated measure predicting the number of patients who would need to be treated to prevent one additional adverse outcome.

Methods

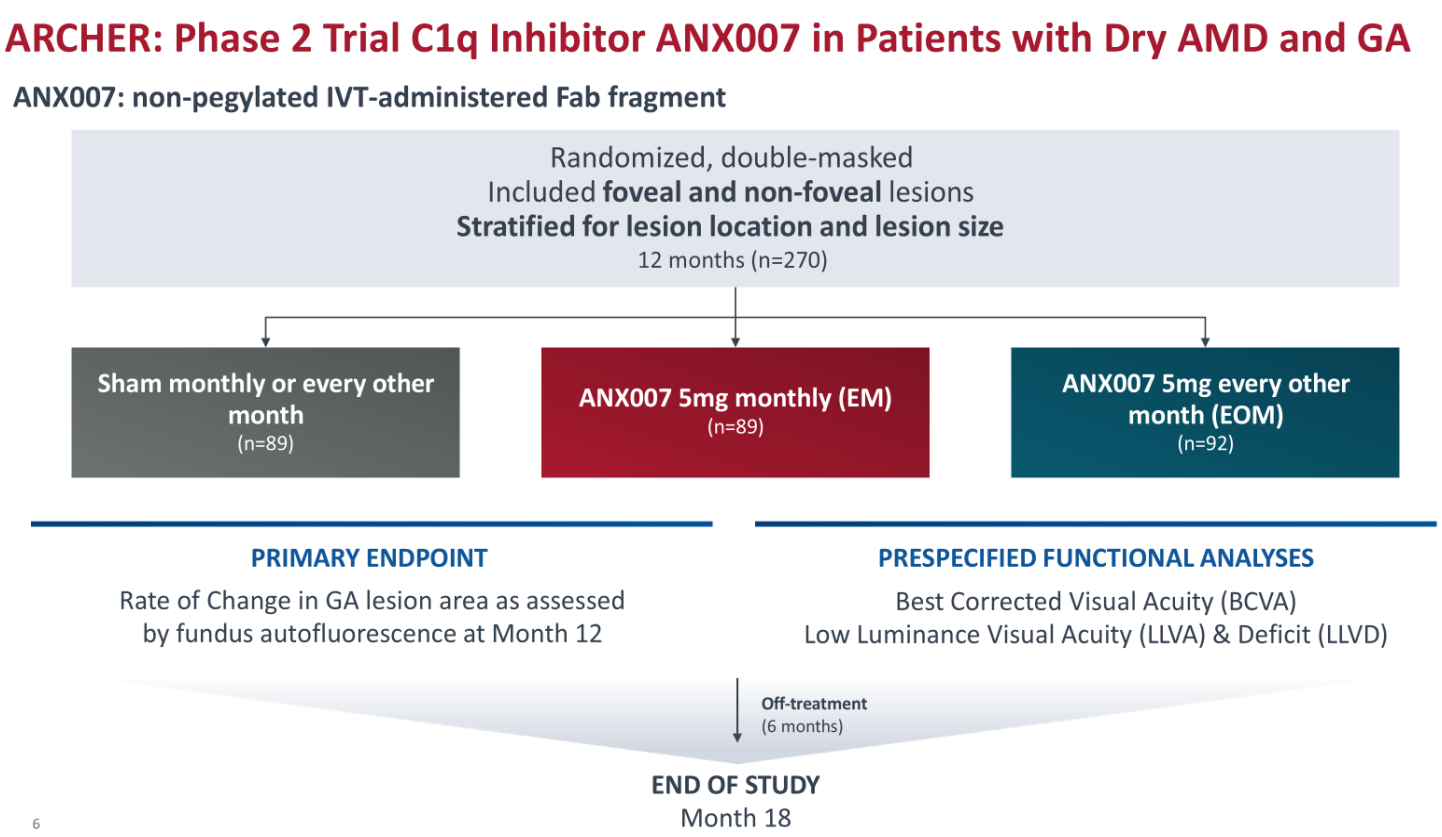
- Participants in ARCHER, a phase 2 randomized trial in participants with dry AMD with Geographic Atrophy, were randomized to receive intravitreal (IVT) administration of 5 mg ANX007 monthly (EM, n=89) or every other month (EOM, n=92), or matched sham (n=89).
- Treatment was administered for 12 months, after which participants were followed for an additional 6 months off treatment.



Methods

- Prespecified analyses included best-corrected visual acuity (BCVA) ≥15-letter loss at 2 consecutive visits and changes from baseline in EZ and RPE structure.

- Additional analyses were conducted to evaluate the effect of ANX007 on these measures in participants with relatively less advanced disease at baseline (less EZ loss and lower low luminance visual deficit [LLVD]).



The Number Needed to treat Analysis was calculated as follows:

$$\frac{1}{\text{(Event Rate in Sham – Event Rate in EM group)}}$$

With results rounded up to the next whole number

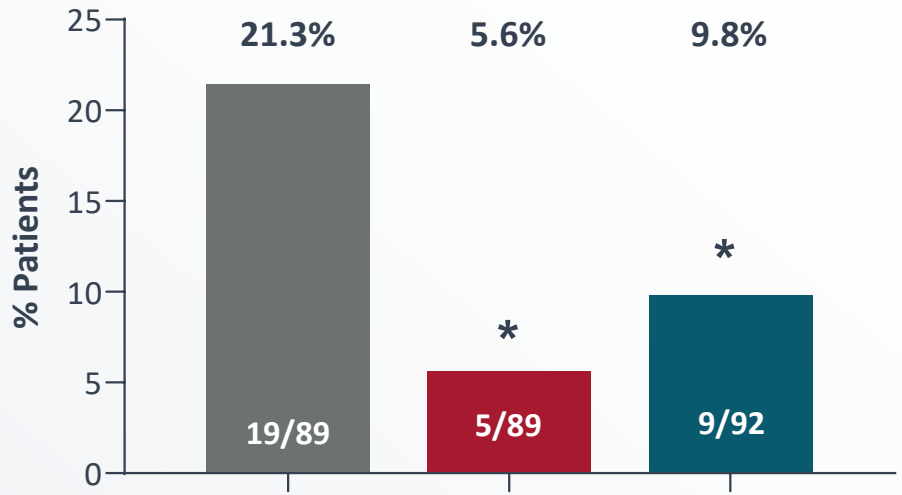
Results: Patient Demographics and Study Eye Baseline Characteristics Were Generally Well-Balanced Across Groups

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%)

Results: Fewer Patients Treated with ANX007 Had Confirmed BCVA ≥15-Letter Loss Through Month 12

A Prespecified Secondary Analysis

PATIENTS WITH CONFIRMED BCVA ≥15-LETTER LOSS THROUGH MONTH 12#



Nominal p-value vs sham^	---	0.0021	0.032

#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

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

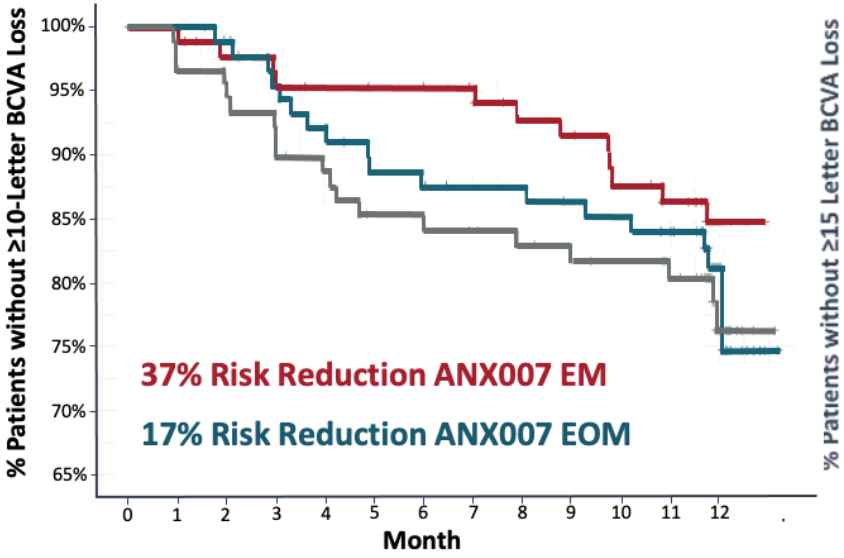
Number Needed to Treat = 7

For every 7 patients treated with ANX007 monthly, 1 additional patient would be spared clinically significant vision loss

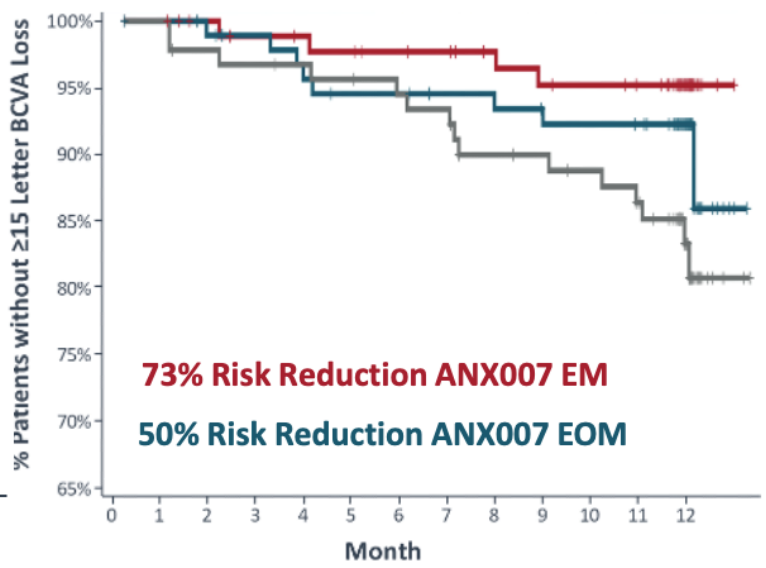
Results: Fewer Patients Treated With ANX 007 Had Confirmed BCVA Loss of ≥10, ≥15, and ≥20 letters Through Month 12

Dose- and Time- dependent protection from BCVA ≥10, ≥15- and ≥20-letter loss

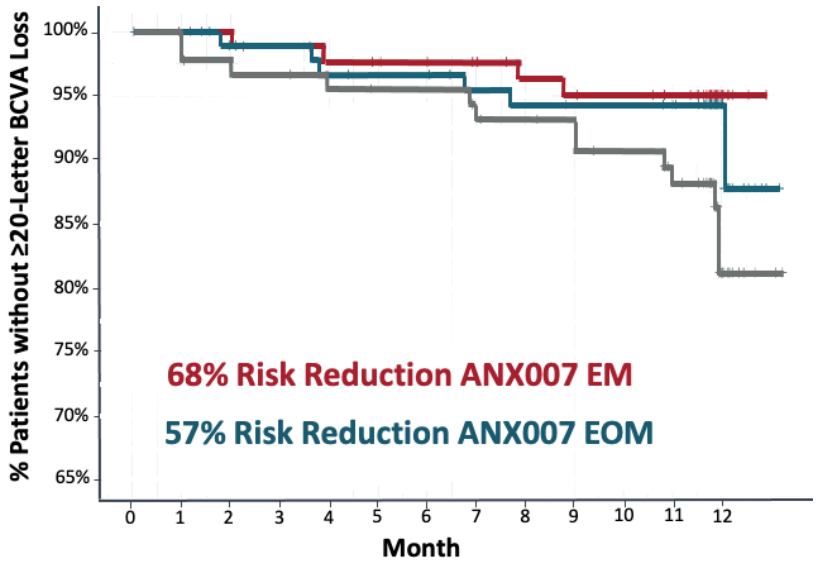
≥10-LETTER LOSS



≥15-LETTER LOSS



≥20-LETTER LOSS



Nominal p-value vs sham^	EM	EOM
≥10-LETTER LOSS	0.1952	0.6015
≥15-LETTER LOSS	0.0098*	0.0788
≥20-LETTER LOSS	0.0330*	0.0841

#Persistent for two consecutive visits through month 12; month 12 confirmed at month 15 visit
^Nominal p-value from a Chi-square test in ITT population
* P < 0.05

Number Needed to Treat EM

To Avoid ≥10 LL = 10

Number Needed to Treat EM

To Avoid ≥15 LL = 7

Number Needed to Treat EM

To Avoid ≥20 LL = 8

Results: Number Needed to Treat

- NNT values of ~6-10 in ARCHER are consistent across measures and compare favorably to other therapeutic area interventions:

NNT = 125 to prevent stroke with statin therapy, in patients with known heart disease [1-3]

NNT = 333 to avoid a nonfatal heart attack as a first cardiovascular event with Aspirin therapy[4-6]

1. Thavendiranathan P. Primary prevention of cardiovascular disease with statin therapy. Arch Int Med. 2006; 166: 2307-13.

2. CTT Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. Lancet. 2005; 366: 1267-1278.

3. Ridker et al. Rosuvastatin to prevent vascular events in men and women with elevated c-reactive protein. NEJM. 2008; 359(21): 2195-2207.

4. Bibbins-Domingo K. Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventative Service Task Force Recommendation Statement. Ann Intern Med. 2016;164:836-845.

5. Mahmoud AN, Gad MM, Elgendy AY, Elgendy IY, Bavry AA. Efficacy and safety of aspirin for primary prevention of cardiovascular events: a meta -analysis and trial sequential analysis of randomized controlled trials. Eur Heart J. 2019;40:607 -17.

6. Zheng SL, Roddick AJ. Association of Aspirin Use for Primary Prevention With Cardiovascular Events and Bleeding Events: A Systematic Review and Meta-analysis. JAMA. 2019;321:277–87.

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
  - **Number Needed To Treat Ranged from 6-10 to prevent additional adverse outcomes across various outcomes measures** with ANX007 EM vs sham

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