ARCHER II, a Global, Double-Masked, Randomized Phase 3 Clinical Trial of Vonaprument (ANX007) in Participants with Dry AMD with GA: Background, Rationale and Study Design

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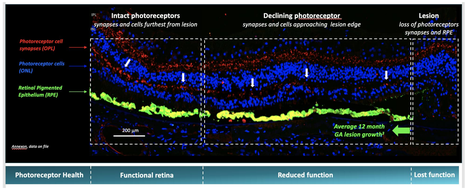
INTRODUCTION

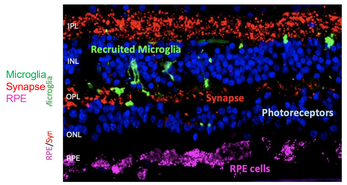
- Activation of the classical complement cascade has been implicated in the pathogenesis of geographic atrophy (GA) and other neurologic diseases
- C1q, the initiating molecule of the classical complement cascade, is a common driver of neurodegeneration
- Inhibition of C1q appears to convey neuroprotective effects across several neurodegenerative diseases
- Vonaprument is an antibody fragment that inhibits C1q and is delivered intravitreally
- The Phase 2 ARCHER study (NCT04656561) compared vonaprument (ANX007) 5mg monthly (EM), vonaprument (ANX007) 5mg every other month (EOM), or sham (EM or EOM)

BACKGROUND

Human GA Retina Tissue



- Photoreceptors and RPE provide bidirectional trophic support to each other
- Ellipsoid zone (EZ) area loss is larger than RPE area loss, RPE loss occurs after EZ loss in dry AMD with GA



- Microglia (labeled in green) are observed in human GA retina
- These microglia attack photoreceptor synapses with disease directly

- Blocking C1q protects structure and function of synapses and photoreceptors[1]

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

ARCHER METHODS & RESULTS

ARCHER Phase 2 Study Design

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)	Vonaprument 5mg monthly (EM) (n=89)	Vonaprument 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)

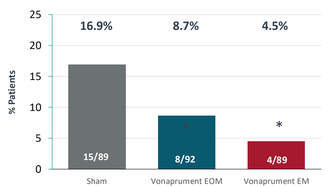
Off-treatment (6 months)

END OF STUDY
Month 18

- 6.2% greater reduction in retinal pigment epithelium (RPE) loss from baseline (EM group vs. sham) at 12 months – did not reach statistical significance (primary)
- Consistent treatment effects observed across visual acuity measures (BCVA, LLVA) support effect of vonaprument in GA
- Preservation of photoreceptor (EZ) structure across the full macular grid and subdomains is supportive of vonaprument vision impact

ARCHER RESULTS

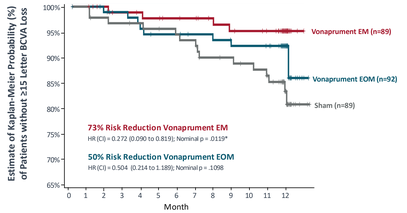
Proportion of Patients with 15-letter BCVA loss



Nominal p-value vs sham^	---	.0994	.0076

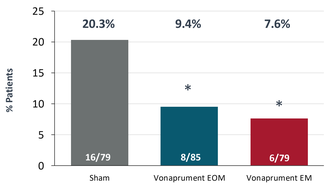
Confirmed at two consecutive visits through month 12 (month 12 supported by month 15 visit)
^Nominal p-value from a Chi-square test in ITT population: *Nominal p < .05

Proportion of Patients Without ≥15-letter BCVA Loss at 2 Consecutive Visits Through Month 12



HR, hazard ratio; Nominal log-rank test (versus sham) p-values are presented;
*Confirmed BCVA 15-LL at two consecutive visits including month 12 supported by month 15 visit
Nominal p-value from a Chi-squared test in ITT population; *Nominal p < .05

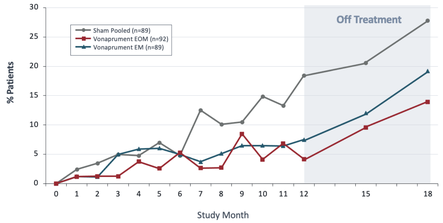
Proportion of Patients with 15-letter LLVA loss



Nominal p-value vs sham^	---	.0497	.0216

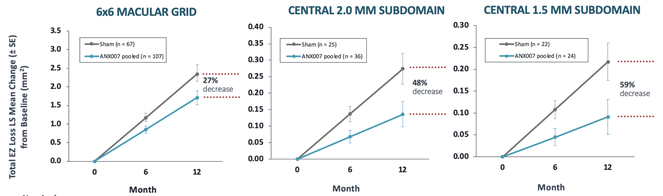
Patients with at least one post-baseline LLVA measurement and two consecutive or last visit 15-letter loss events ; ^Nominal p-value from a Chi Square test; *Nominal p < .05

Proportion of Patients With Single Visit ≥15-letter BCVA Loss Through Month 18, Including Off Treatment Period



Single visit 15-letter loss events through month 18 loss (at month 12 was confirmed at the month 15 visit)

LS Mean Change from Baseline in Total Ellipsoid Zone (EZ) Loss Through 12 Months



Nominal p-value^	ANX007 Pooled vs Sham .0472	ANX007 Pooled vs Sham .0242	ANX007 Pooled vs Sham .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;

Key Safety Data from ARCHER

ADVERSE EVENTS OF SPECIAL INTEREST n (%)	SHAM (N=89)	VONAPRUMENT EM (N=89)	VONAPRUMENT 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

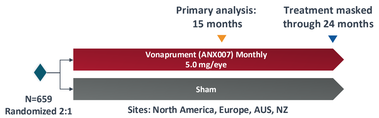
Vitritis – 1
Resolved with topical steroids in 9 days
No Vasculitis

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

*Event Verbatim term listed

ARCHER II PHASE 3 PROGRAM

ARCHER II Design



- Primary endpoint: Proportion of eyes with confirmed* BCVA ≥15-letter loss through primary analysis timepoint
  - *Defined as ≥15-letter loss confirmed at two consecutive visits
- Secondary endpoints: Safety, LLVA, LLVD, EZ integrity
- Study Population: Comparable to ARCHER; foveal and non-foveal lesions included; history of CNV in fellow eye permitted; eyes with <45 letters at baseline are excluded
- ARCHER II is fully enrolled; data expected 4Q 2026

CONCLUSIONS

- ARCHER results suggest that C1q inhibition with vonaprument conveys a drug-related photoreceptor protective effect that may explain associated prevention of visual acuity loss
- Inhibition with C1q conveys neuroprotective effects, suggesting the anti-C1q therapy may provide neuroprotection against inflammation and neuronal damage and loss induced by downstream complement components
- Vonaprument has the potential to be the first pharmacologic treatment preserve vision in patients with GA

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Poster presented by Simona Degli Esposti, MD email: s.esposti@nhs.net at the Royal College of Ophthalmologists Annual Congress, May 18-21, 2026