Vision Outcomes in Eyes with Subfoveal RPE Lesions in Geographic Atrophy: A Post Hoc Analysis of the Phase 2 ARCHER Trial

Poster #23

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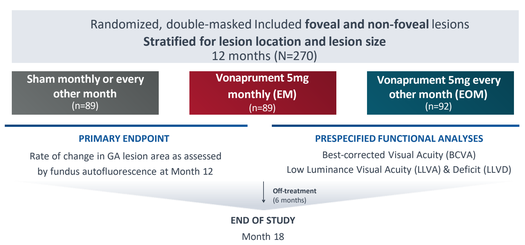
INTRODUCTION

- 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
- ARCHER (NCT04656561) compared vonaprument (ANX007) 5mg monthly (EM) or every other month (EOM) and sham
- Vonaprument is an antibody fragment delivered intravitreally that inhibits C1q
- Recent data indicate that the historic assumption that patients with subfoveal lesions have a lower rate of vision loss than those with non-subfoveal lesions is not accurate[1]
- A recent assessment of the Phase 3 lampalizumab data demonstrated that eyes were still capable of experiencing a clinically significant loss of BCVA even if there was subfoveal involvement[2]
- This analysis considered visual acuity outcomes for the subpopulation with subfoveal lesions at baseline

ARCHER METHODS

ARCHER Phase 2 Study Design

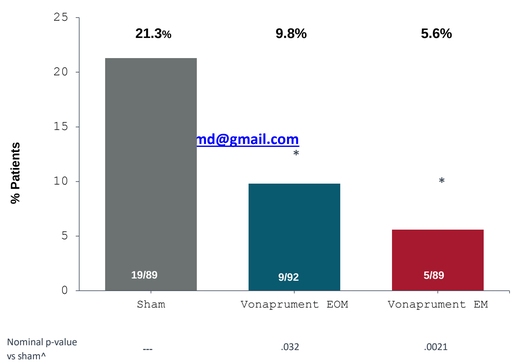


- Subfoveal RPE lesions at baseline:
  - Sham 44/89 (49.4%)
  - Vonaprument EM 49/89 (57.3%)
  - Vonaprument EOM 51/92 (53.3%)
- Baseline characteristics were well balanced across the treatment groups, generally similar by lesion location
- 15-letter loss definition:
  1) Two consecutive visits or last visit

ARCHER RESULTS

- 6.2% greater reduction in rate of change in retinal pigment epithelium (RPE) loss from baseline with vonaprument treatment vs. sham at 12 months – not statistically significant (primary)
- Consistent treatment effects observed across visual acuity measures (BCVA, LLVA) in overall population support effect of vonaprument in GA

Proportion of Patients With ≥15-Letter BCVA Loss In Overall ARCHER Population

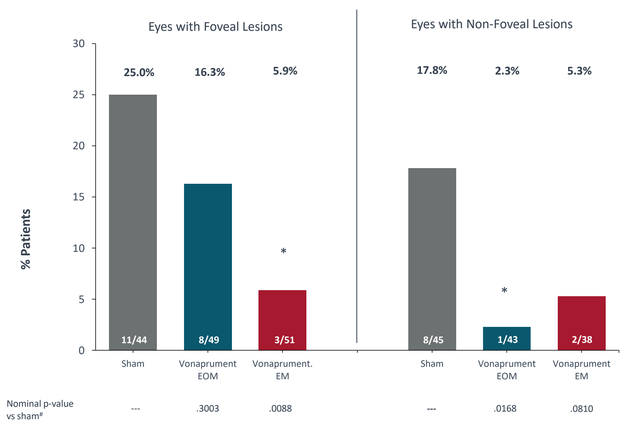


Nominal p-value vs sham^	---	.032	.0021

#Confirmed 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 < .05; Final data

ARCHER RESULTS

Proportion of Patients With ≥15-Letter BCVA Loss by Lesion Location at Baseline



Nominal p-value vs sham#	---	.3003	.0088	---	.0168	.0810

Nominal p-values for treatment arms vs. sham^

Vonaprument EM (all patients)	.0019
Vonaprument EOM (all patients)	.0254

^Nominal p-value from a Cochran-Mantel-Haenszel test (General Association) in overall population; Final data

Confirmed two consecutive visits at any time through month 12 or at last study visit
#Nominal p-value from a Chi-square test population in relevant lesion location subpopulation; Final data

Meta-Analysis Assessment (Forest Plot): Influence of Baseline Characteristics on ≥15-Letter BCVA Loss

*Confirmed for two consecutive visits through month 12 or at last visit; Hazard ratios are from Cox regressions accounting for event time and censorship
NOTE: Hazard ratio not estimated for ANX007 EM vs Sham with baseline LLVD < 30 due to zero (0) event in ANX007 EM group for the subgroup: Final data

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

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

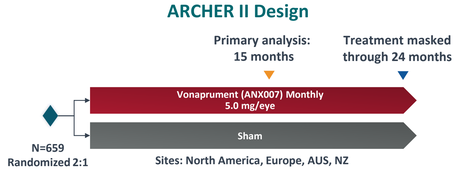
Vitreous Debris – 1
KP on endothelium, prior treatment with topical steroids
No Vasculitis

*Event Verbatim term listed

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

ARCHER II PHASE 3 PROGRAM

ARCHER II Design



Fast Track designation (FDA)

PRIME designation (EMA)*

*Also selected by EMA for Product Development Coordinator program

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

REFERENCES

1. Sunness JS, Gonzalez-Baron J, Applegate CA, Bressler NM, Tian Y, Hawkins B, Barron Y, Bergman A. *Enlargement of atrophy and visual acuity loss in the geographic atrophy form of age-related macular degeneration,* Ophthalmology. 1999 Sep;106(9):1768-79. doi: 10.1016/S0161-6420(99)90340-8

2. Anegondi N, Steffen V, Sadda SR, Schmitz-Valckenberg S, Tufail A, Csaky K, Lad EM, Kaiser PK, Ferrara D, Chakravarthy U. *Visual Loss in Geographic Atrophy: Learnings From the Lampalizumab Trials*, Ophthalmology. 2025 Apr; 132(4):420-430. doi: 10.1016/j.ophtha.2024.11.017

CONCLUSIONS

- This analysis demonstrates that eyes with subfoveal RPE lesions can experience clinically meaningful vision loss over 12 months, consistent with recent reports
- Eyes treated with vonaprument lost meaningfully less vision through 12 months compared to sham in 15-letter loss assessments of BCVA irrespective of lesion location
- Treatment effect, dose response, and statistical results were generally consistent with outcomes for the overall population in ARCHER
- Vonaprument has the potential to be the first pharmacologic treatment to preserve vision in patients with GA
- The ongoing phase 3 ARCHER II program in eyes with dry AMD with GA enrolled both subfoveal and non-subfoveal lesions at baseline
- Data are expected in 4Q 2026

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