Primary Endpoint Results from a Prospective, Randomized Pivotal Clinical Trial of Avacincaptad Pegol in the Treatment of Geographic Atrophy

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Disclosures

- Research Grant Support: Genentech, Regeneron, Novartis, Allergan, Astellis, Notal, Chengdu Kanghong, Opthea, IVERIC Bio, Adverum, RegenXBio, Kodiak, Graybug

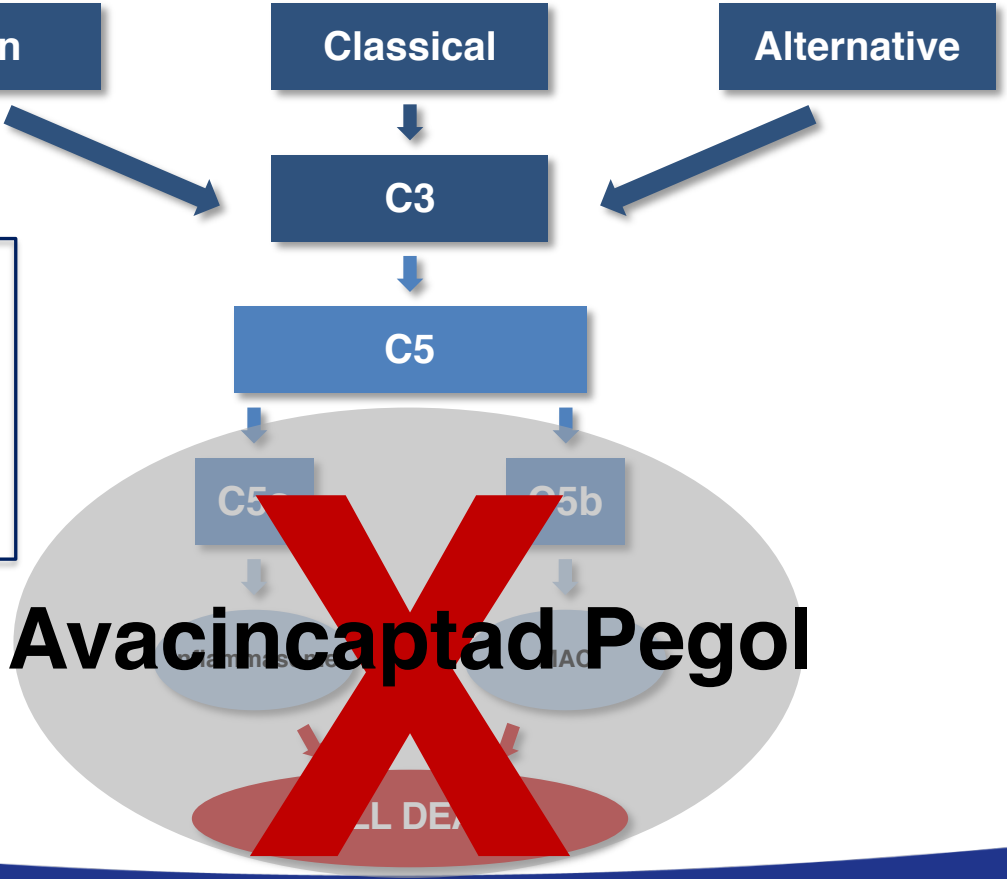
- Consulting: Genentech, Novartis, Allergan, Notal, Iconic, Takeda, Kodiak, Graybug, Lineage, Opthea, Eyepoint, IVERIC bio, Aldeyra, Merck, Adverum, Chengdu Kanghong

Summary: GATHER1 Phase 3 Pivotal Clinical Trial

- Primary efficacy endpoint was achieved for both avacincaptad pegol 2 mg and 4 mg dose, leading to a statistically significant ~27% reduction in GA growth over 12 months
  - Reduction in GA growth (~26-28%) observed at 6 months for both avacincaptad pegol 2 mg and 4 mg*
  - Sham arm performed as expected
  - 18 month outcomes continue to show benefit in GA reduction
- Safety: Both avacincaptad pegol 2 mg and 4 mg were well tolerated over 12 months
- The confirmatory pivotal phase 3 clinical trial (GATHER2) launched: Avacincaptad pegol 2 mg vs Sham

* Descriptive analysis based on MRM model; not pre-specified

Complement Pathway: Inflammasome & MAC X Cell Death



Avacincaptad Pegol

- 39-mer – oligonucleotide conjugated to 40 kDa PEG
- Formulation: sterile, preservative free solution for intravitreal injection (100 µL)

Phase 3 Pivotal Clinical Trial for GA Secondary to AMD

GATHER1 Clinical Trial

A Randomized, Double-Masked, Sham Controlled Trial to Assess the Safety and Efficacy of Intravitreal Administration of Avacincaptad Pegol in Subjects with Geographic Atrophy Secondary to Age-Related Macular Degeneration (AMD)

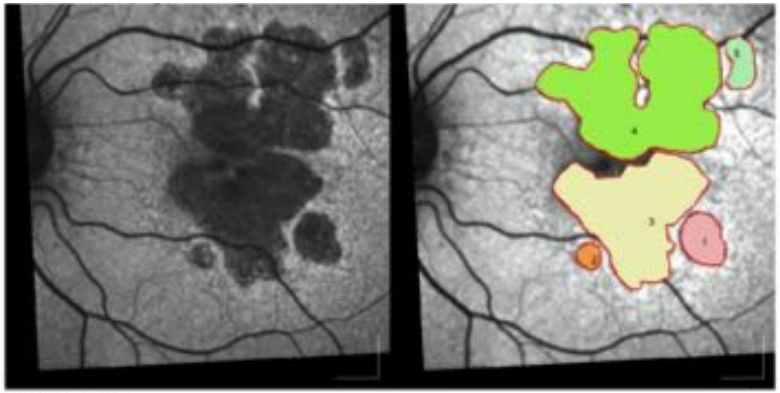
Avacincaptad pegol in GA Secondary to AMD Pivotal Clinical Trial

- Randomized, double masked, sham controlled clinical trial
- Cohorts included in the pre-specified statistical analysis of the primary endpoint at Month 12*:
  - Avacincaptad pegol 4 mg dose
  - Avacincaptad pegol 2 mg dose
  - Sham
- 286 subjects were enrolled for monthly treatment with avacincaptad pegol or Sham for 18 months
  - ~75% of the patients were enrolled in the US

*Descriptive analysis was performed for the avacincaptad pegol 1mg cohort

Primary Efficacy Endpoint

Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation of GA lesion)

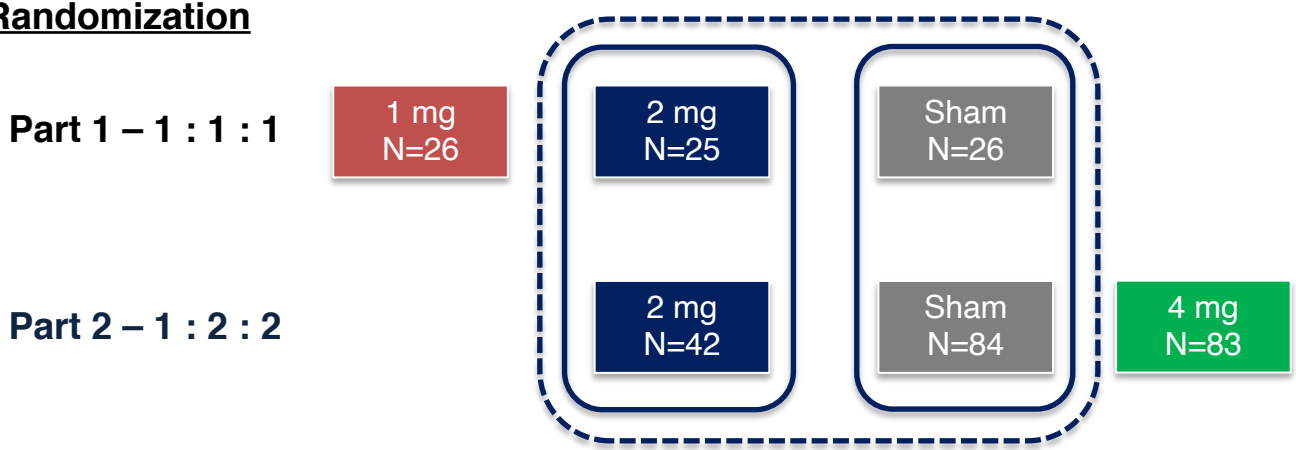


Duke Reading Center

Avacincaptad Pegol in GA Secondary to AMD Clinical Trial

Masked Throughout the Entire process

Randomization



Efficacy Evaluation Based on Prespecified Statistical Analysis Plan (SAP):

- Avacincaptad pegol 2 mg vs. Sham: subjects randomized from Part 1 were combined with the subjects randomized from Part 2, where the analysis included a regression factor by part

Avacincaptad Pegol in GA Secondary to AMD Clinical Trial

Randomization

Masked Throughout the Entire process

Part 1 – 1 : 1 : 1

- 1 mg N=26
- 2 mg N=25
- Sham N=26

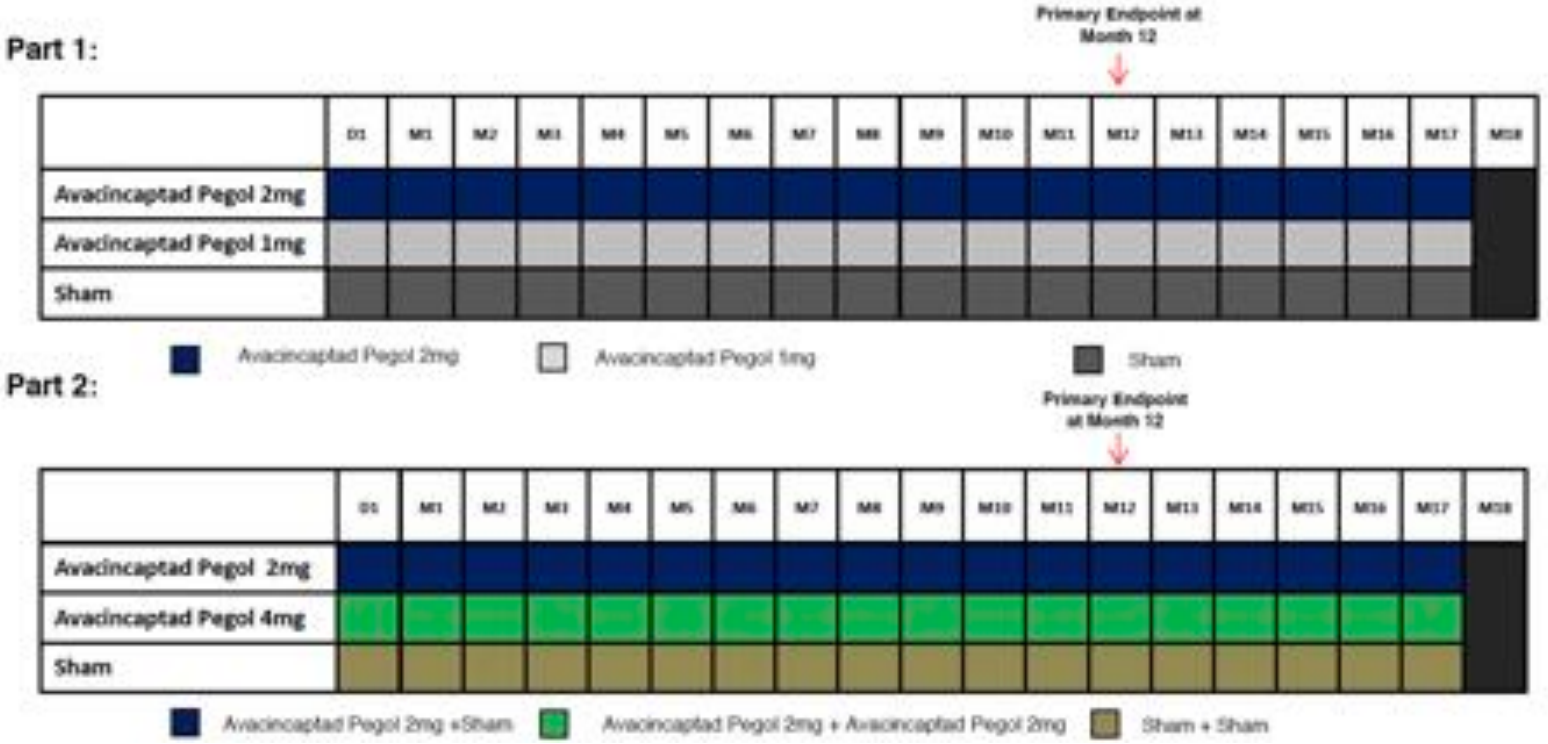
Part 2 – 1 : 2 : 2

- 2 mg N=42
- Sham N=84
- 4 mg N=83

Efficacy Evaluation

- Avacincaptad pegol 4 mg vs. Sham: based only on subjects randomized in Part 2

Avacincaptad Pegol in GA Secondary to AMD Clinical Trial



* Avacincaptad 4 mg was 2 injections

Key Ophthalmic Inclusion Criteria (Study Eye)

- Non-foveal GA secondary to dry AMD
- Total GA area ≥ 2.5 and ≤ 17.5 mm^2 (1 and 7 disk areas [DA] respectively), determined by screening images of FAF
- If GA is multifocal, at least one focal lesion should measure ≥ 1.25 mm^2 (0.5 DA)
- GA in part within 1500 microns from the foveal center
- The atrophic lesion must be able to be photographed in its entirety
- Best corrected visual acuity (BCVA) study eye: 20/25 – 20/320 (Snellen equivalent)

Key Ophthalmic Exclusion Criteria

- GA secondary to any condition other than AMD in either eye (e.g., drug-induced)
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye, except oral supplements of vitamins and minerals
- Evidence of CNV in either eye. If CNV develops in the SE during the course of the study, the subject were withdrawn from the study
- Any ocular condition in the SE that would progress during the course of the study that could affect central vision or otherwise be a confounding factor

Baseline Characteristics

	Avacincaptad Pegol 2 mg N = 67	Sham for 2 mg arm N = 110	Avacincaptad Pegol 4 mg N = 83	Sham for 4 mg arm N = 84
Mean Age, Years	78.8	78.2	79.2	78.2
Female Gender, Number (%)	45 (67.2%)	79 (71.8%)	58 (69.9%)	61 (72.6%)
Active smoker, Number (%)	25 (37.3%)	36 (32.7%)	26 (31.3%)	29 (34.5%)
Non-Subfoveal GA, Number (%)	62 (92.5%)	104 (94.5%)	81 (97.6%)	82 (97.6%)
Mean GA Area, mm^2	7.33	7.42	7.90	7.45
Mean SQ Root GA Area, mm	2.62	2.63	2.72	2.64
Bilateral GA, Number (%)	67 (100%)	108 (98.2%)	83 (100%)	83 (98.8%)
Hyper Autofluorescence (%)	66 (98.5%)	109 (99.1%)	82 (98.8%)	83 (98.8%)
Mean BCVA (ETDRS Letters)	70.2	69.0	69.5	68.3
Mean LL BCVA (ETDRS Letters)	36.7	34.5	36.8	33.9
Low Luminance Deficit (BCVA-LL BCVA)	33.5	34.5	32.7	34.4

Balanced Across Cohorts

Primary Efficacy Endpoint Results

Mean Rate of Change in Geographic Atrophy Area from Baseline to Month 12

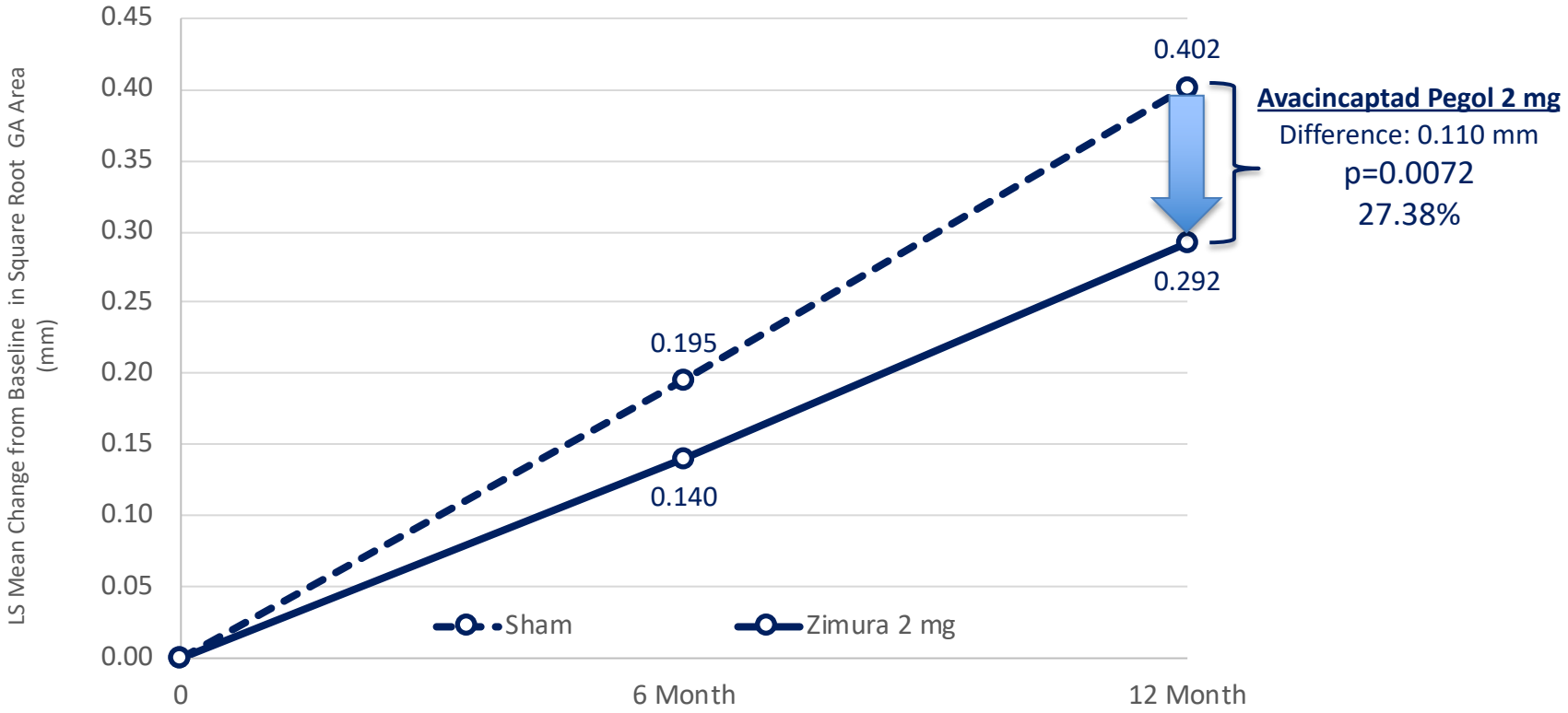
Square Root Transformation, ITT Population

Cohort	Avacincaptad Pegol 2 mg (N = 67)	Sham 2 mg (N = 110)	Difference	P-value	% Difference
Mean Change in GA[a] (mm)	0.292 [c]	0.402 [c]	0.110	0.0072 [b]	27.38%

Cohort	Avacincaptad Pegol 4 mg (N = 83)	Sham 4 mg (N = 84)	Difference	P-value	% Difference
Mean Change in GA[a] (mm)	0.321	0.444	0.124	0.0051 [b]	27.81%

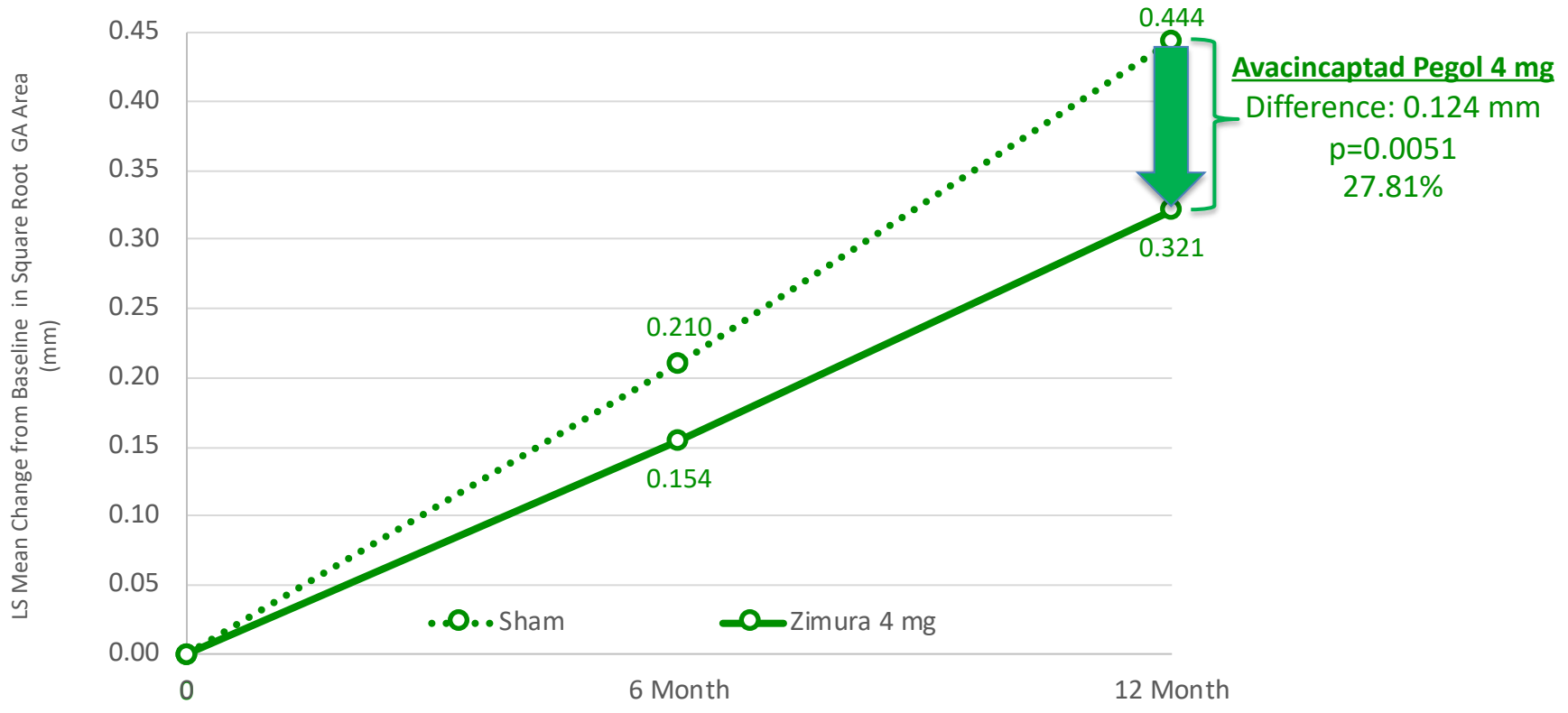
(b) = reflects statistically significant p-value; Hochberg procedure was used for significance testing
(c) = these least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data

Primary Efficacy Endpoint: Avacincaptad Pegol 2 mg vs. Sham



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing. These least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.

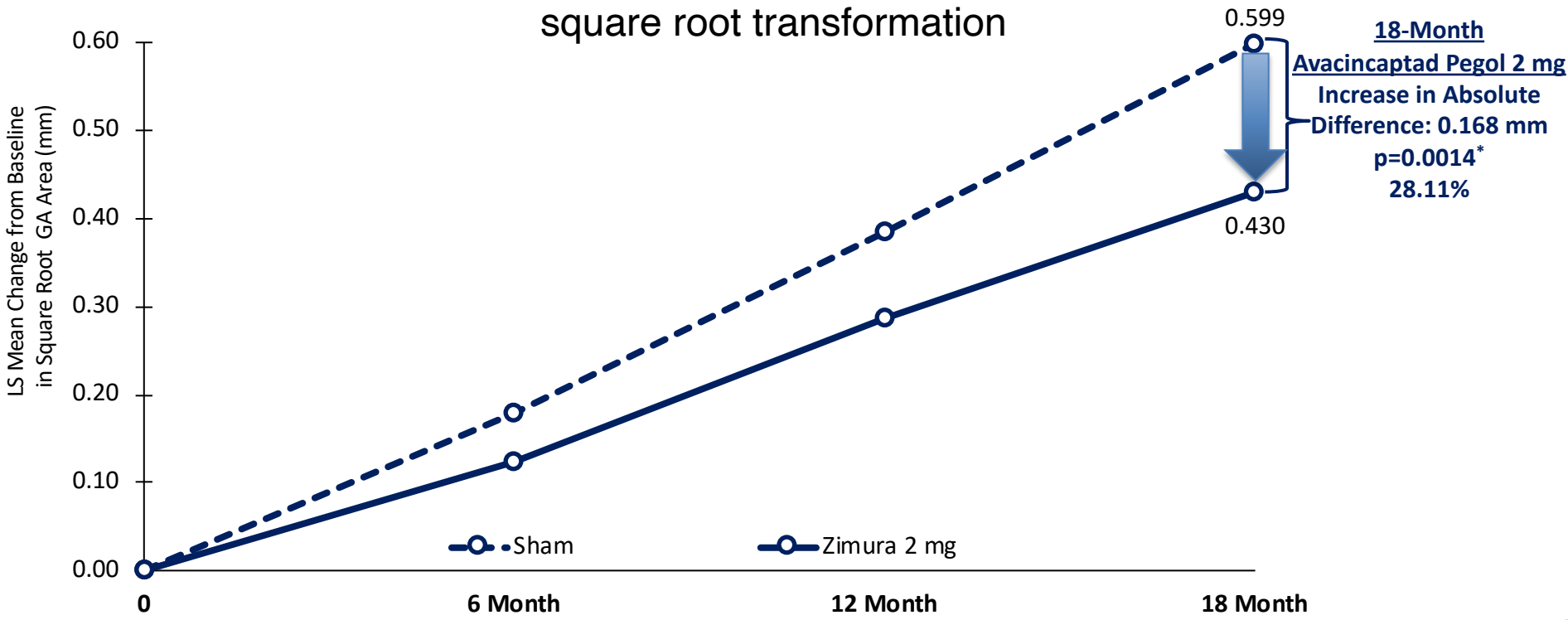
Primary Efficacy Endpoint: Avacincaptad Pegol 4 mg vs. Sham



Based on LSMEANS from MRM Model; ITT Population Hochberg procedure used for significance testing

18 Month Results

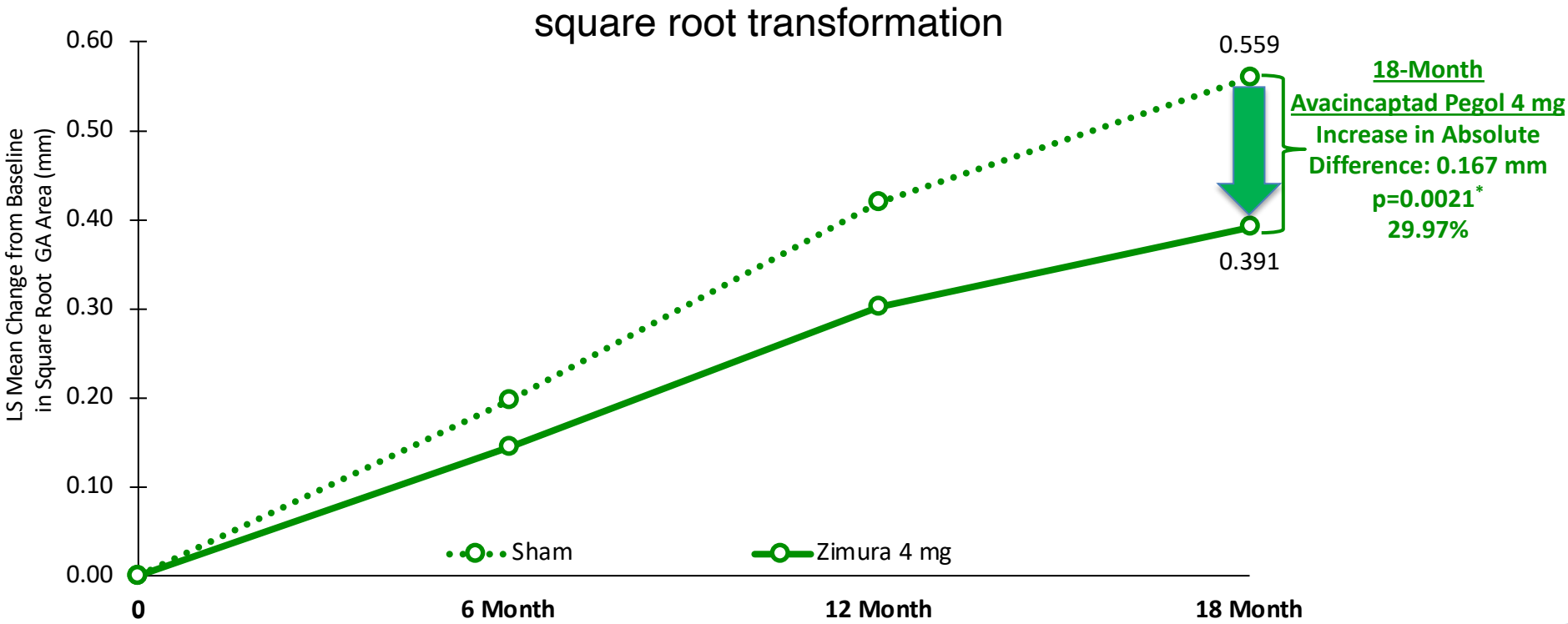
Avacincaptad Pegol 2 mg vs. Sham



ITT Population; Based on LSMEANS from MRM Model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data; Prespecified and descriptive analysis. *18 month p values are descriptive in nature.

18 Month Results

Avacincaptad Pegol 4 mg vs. Sham



ITT Population; Based on the least squares means from the MRM Model drawing on all available data; Prespecified and descriptive analysis. *18 month p values are descriptive in nature.

Secondary Endpoints

Trial not designed to demonstrate differences in mean changes in BCVA or LL BCVA with statistical significance

- Mean change in best corrected visual acuity (ETDRS letters) from Baseline to Month 12

Cohort	Avacincaptad Pegol 2mg (N=67)	Sham (N=110)	Difference
Mean Change in BCVA[a]	-7.90[b]	-9.29[b]	1.39

Cohort	Avacincaptad Pegol 4mg (N=83)	Sham (N=84)	Difference
Mean Change in BCVA[a]	-3.79	-3.51	-0.28

- Mean change in low luminance best corrected visual acuity (ETDRS letters) from Baseline to Month 12

Cohort	Avacincaptad Pegol 2mg (N=67)	Sham (N=110)	Difference
Mean Change in LL BCVA[a]	-1.03[b]	-1.41[b]	0.38

Cohort	Avacincaptad Pegol 4mg (N=83)	Sham (N=84)	Difference
Mean Change in LL BCVA[a]	1.53	2.97	-1.44

(a) Based on the least square means from the MRM model; ITT population.

(b) These least square means are estimates of the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.

Safety: Through Month 12

- Avacincaptad pegol was generally well tolerated after 12 months of administration
- No avacincaptad pegol related adverse events
- No avacincaptad pegol related inflammation
- No drug related discontinuations from the trial attributed to avacincaptad pegol
- No serious ocular adverse events in the study eye
- No cases of endophthalmitis reported in the clinical trial
- The most frequently reported ocular adverse events were related to the injection procedure
- Incidence of CNV in the untreated fellow eyes was 10 patients (3.5%) and in the study eyes was 3 patients (2.7%) in the sham group, 1 patient (4.0%) in the avacincaptad pegol 1mg group, 6 patients (9.0%) in the avacincaptad pegol 2mg group, and 8 patients (9.6%) in the avacincaptad pegol 4mg group

Favorable Safety Profile To Date

Conclusions

Pivotal Clinical Trial Highlights

- Randomized, double masked, multi-national, sham controlled clinical trial
- Robust independent imaging and prespecified statistical analysis plan
- Primary efficacy endpoint was achieved for both avacincaptad pegol 2 mg and 4 mg dose, leading to a ~27% reduction in GA growth over 12 months
  - Reduction in GA growth (~26-28%) observed already at 6 months in both avacincaptad pegol 2 mg and 4 mg groups*
  - Sham arm performed as expected
  - 18 month outcomes continue to show benefit in GA reduction
- Safety: Both avacincaptad pegol 2 mg and 4 mg were well tolerated over 12 months
- The confirmatory pivotal clinical trial: Compare avacincaptad pegol 2 mg vs Sham

* Descriptive analysis based on MRM model; not pre-specified

GATHER2 Clinical Trial

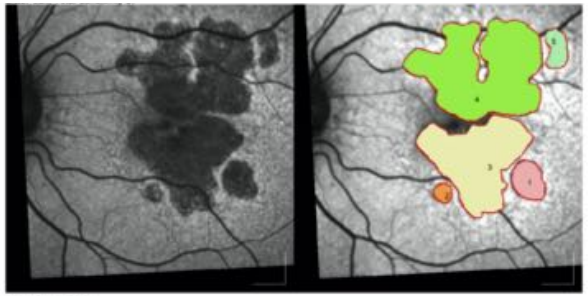
A Phase 3 Multicenter, Randomized, Double-masked, Sham Controlled Clinical Trial to Assess the Safety and Efficacy of Intravitreal Administration of Avacincaptad Pegol in Subjects with Geographic Atrophy Secondary to Age-related Macular Degeneration

Avacincaptad Pegol in GA Secondary to AMD Pivotal Clinical Trial

- ~ 400 subjects will be enrolled for treatment with avacincaptad pegol 2 mg or Sham for 24 months
- Two Arms, 1:1 Randomization:

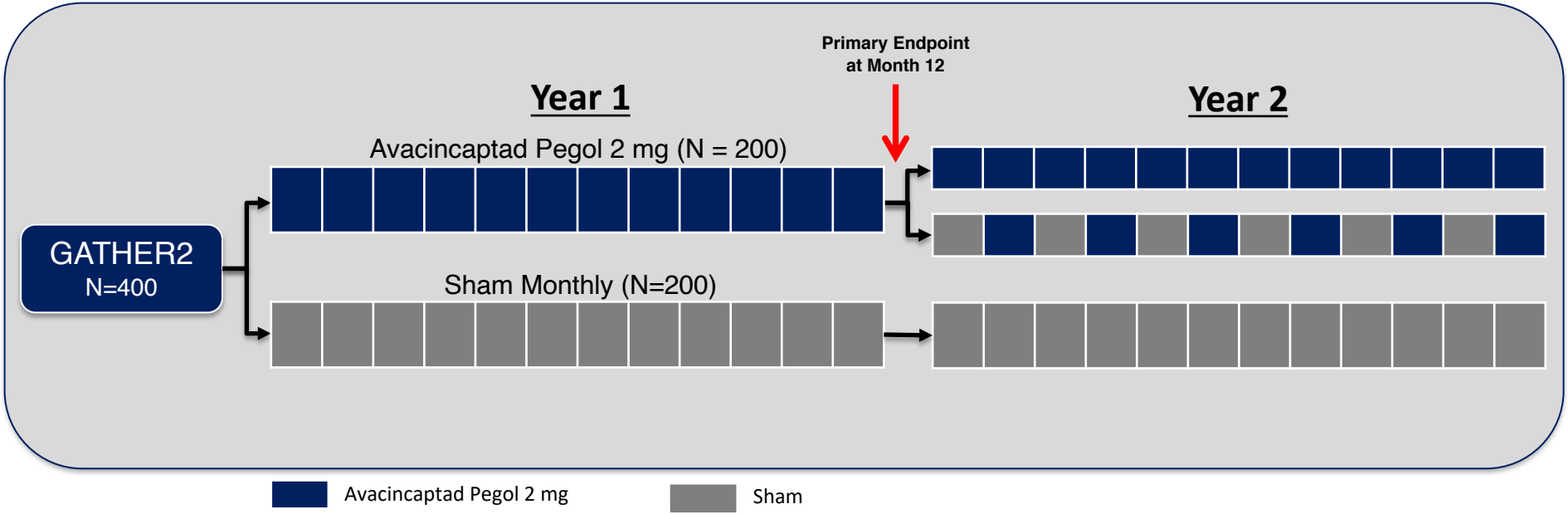
Avacincaptad Pegol 2 mg N=200	Sham N=200

- **Primary Efficacy Endpoint:**
  - Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation of GA lesion)



Avacincaptad Pegol in GA Pivotal Clinical Trial

Primary Efficacy Endpoint: Mean rate of change in GA over 12 months measured by fundus autofluorescence (FAF) at three time points: Baseline, Month 6, and Month 12 (square root transformation)



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- If GA is multifocal, at least one focal lesion should measure ≥ 1.25 mm^2 (0.5 DA)
- GA in part within 1500 microns from the foveal center
- The atrophic lesion must be able to be photographed in its entirety
- Best corrected visual acuity in the SE between 20/25 – 20/320, inclusive

Key Ophthalmic Exclusion Criteria

- GA secondary to any condition other than AMD in either eye (e.g., drug-induced)
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye, except oral supplements of vitamins and minerals
- Evidence of CNV in either eye
- If subject develops CNV in the SE during the course of the trial, the subject remains in the study and continues to receive avacincaptad pegol/Sham treatment (in addition to the standard of care anti-VEGF)
- Any ocular condition in the SE that would progress during the course of the study that could affect central vision or otherwise be a confounding factor

Thank You!