ONS-5010 (bevacizumab-vikg) versus Ranibizumab for Neovascular Age-related Macular Degeneration: Results from the NORSE-EIGHT Noninferiority Randomized Trial

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ONS-5010 (bevacizumab-vikg)

ONS-5010 is an ophthalmic intravitreal formulation of bevacizumab being developed to treat retinal diseases such as wet AMD, DME, and macular edema from BRVO[1]

ONS-5010 has the potential to become the first FDA-approved bevacizumab for ophthalmic use if approved and is manufactured in the United States
ONS-5010 (LYTENAVA™) currently has Marketing Authorization in the European Union and the United Kingdom

ONS-5010 is not a biosimilar, as there is no approved bevacizumab originator product for retinal use

ONS-5010 was studied for administration intravitreally and dosed monthly in clinical trials

1. Summary of Product Characteristics (SmPC) – Lytenava (Bevacizumab gamma). Outlook Therapeutics. Accessed via https://ec.europa.eu/health/documents/community-register/2024/20240527162457/anx_162457_en.pdf

VEGF: Vascular Endothelial Growth Factor. mAB: Monoclonal antibody. HCP: Healthcare provider. GMP: Good manufacturing process. PHSA: public health service act.

ONS-5010 (bevacizumab-vikg) development

Completed

Clinical
Experience Trial

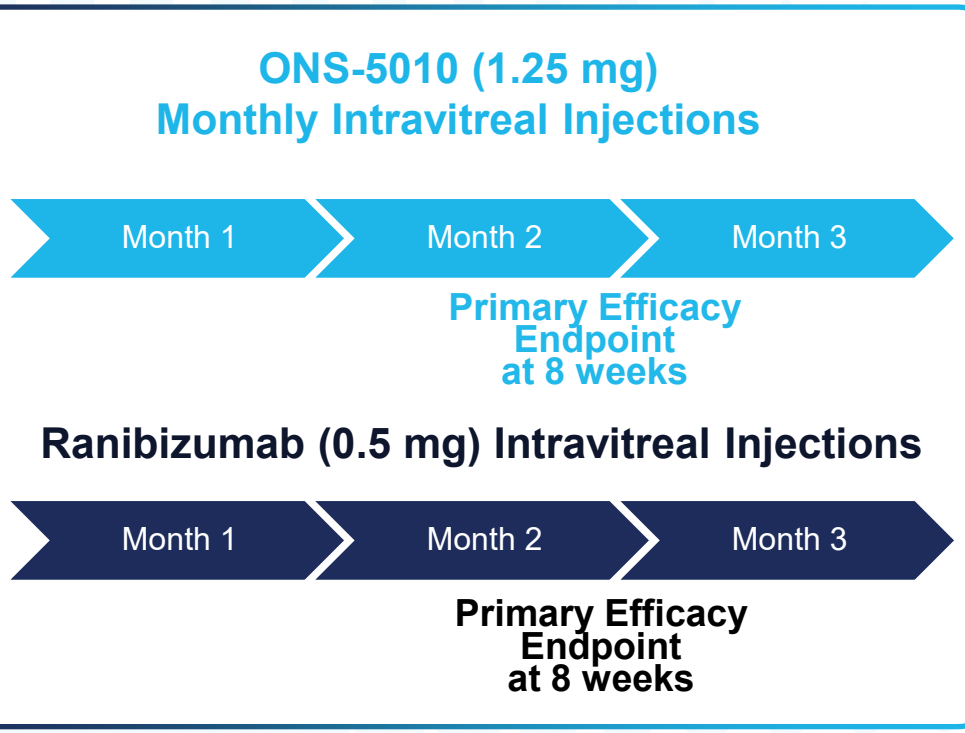
Phase 3
Safety and Efficacy Trial

Open-Label
Safety Study

3-Month Non-Inferiority Study with 8-Week Efficacy Endpoint
Per Special Protocol Assessment (SPA) Agreed with FDA

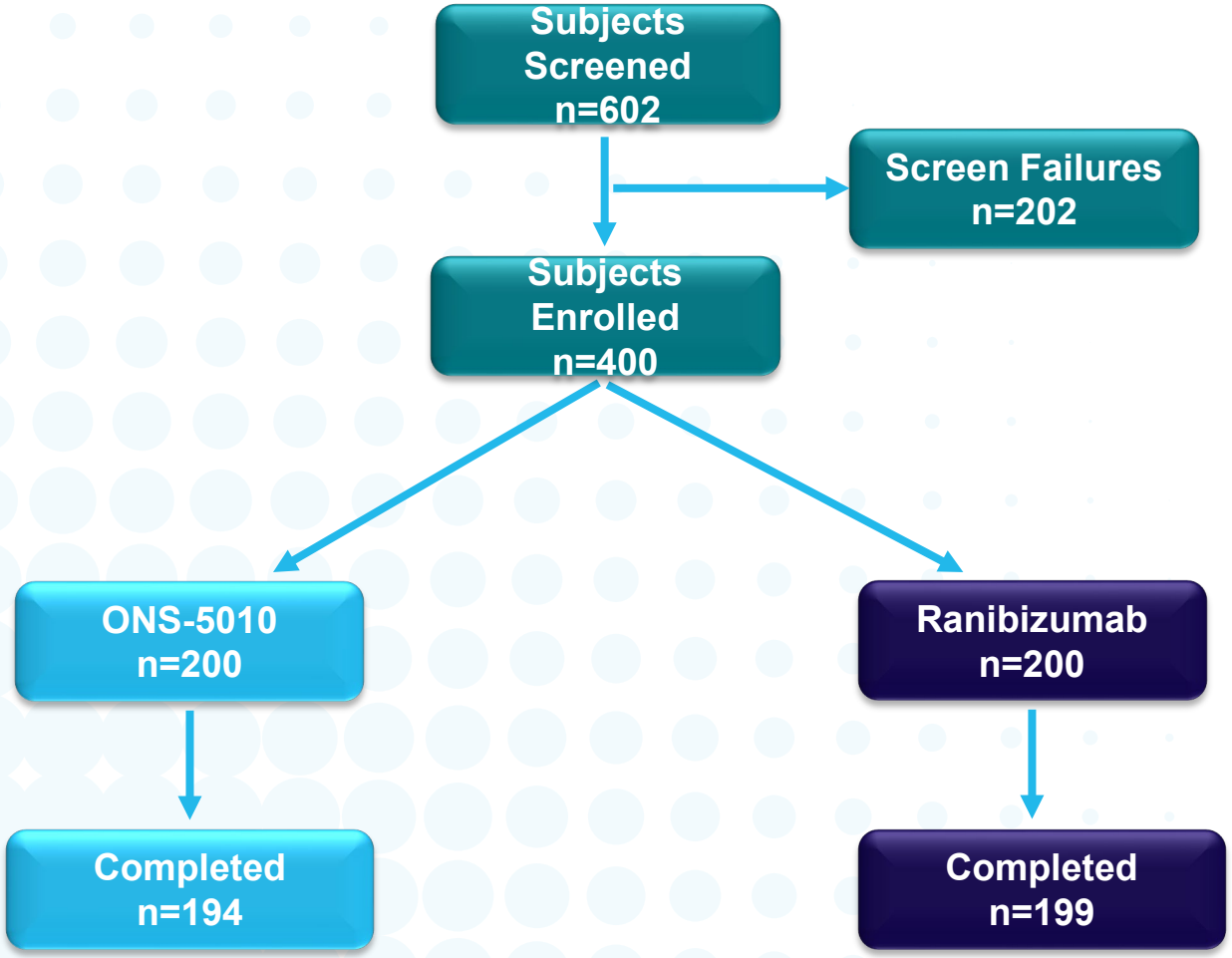
Phase 3 Non-Inferiority Study

Safety and Effectiveness of ONS-5010 Compared to Ranibizumab in Subjects with Neovascular Age-related Macular Degeneration



- Study design mirrors first three months of the positive NORSE TWO Phase 3 study
- 400 treatment naïve, wet AMD subjects enrolled at 61 US sites
- BCVA: 20/32 – 20/200

Randomization

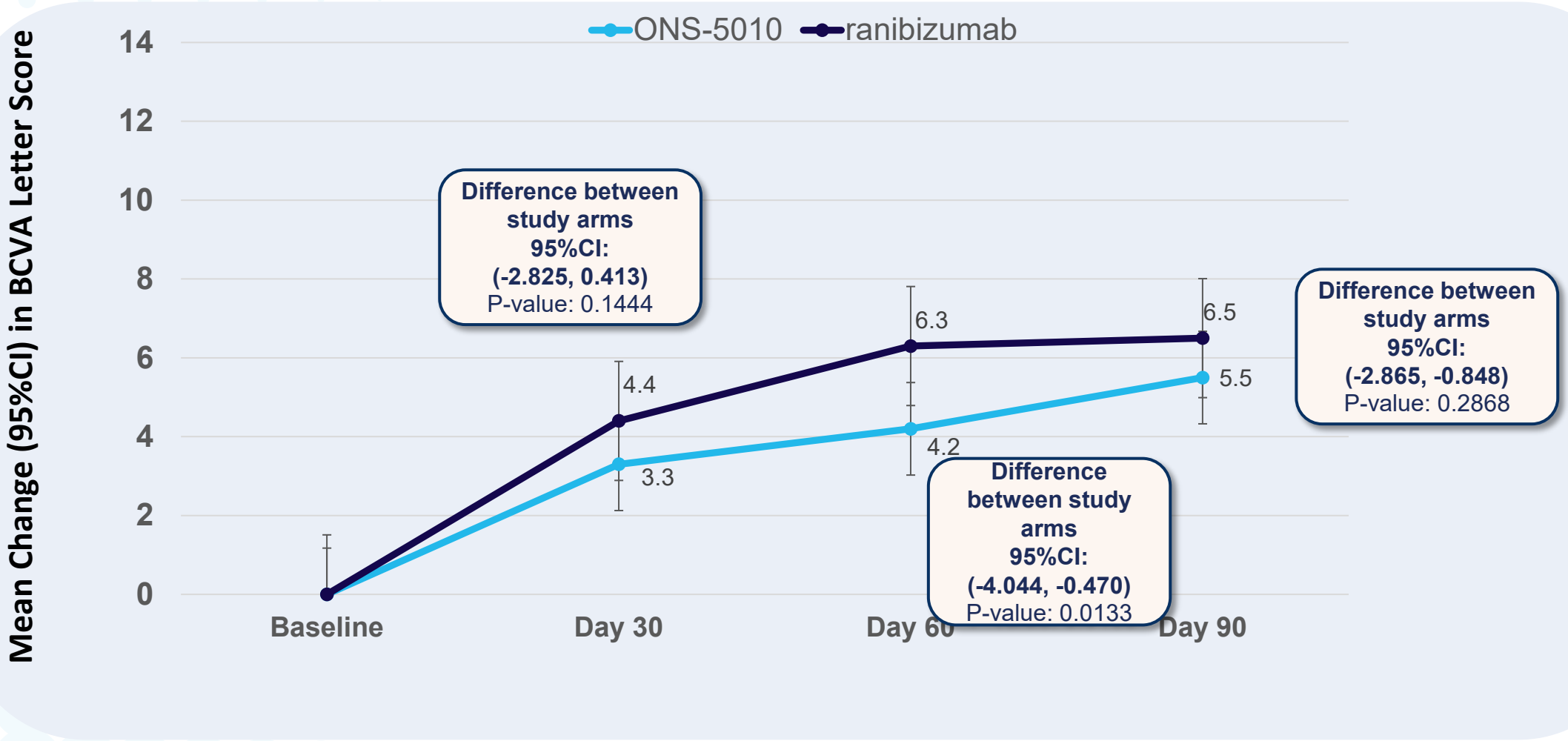


Parameters	ONS-5010 n=200	Ranibizumab n=200
Reason for Early Discontinuation	**6 (3.0%)**	**1 (0.5%)**
Subject withdrew consent	1 (0.5)	0
Adverse event	4 (2.0)	1 (0.5)
Lost to follow-up	1 (0.5)	0

Demographic and Baseline Characteristics

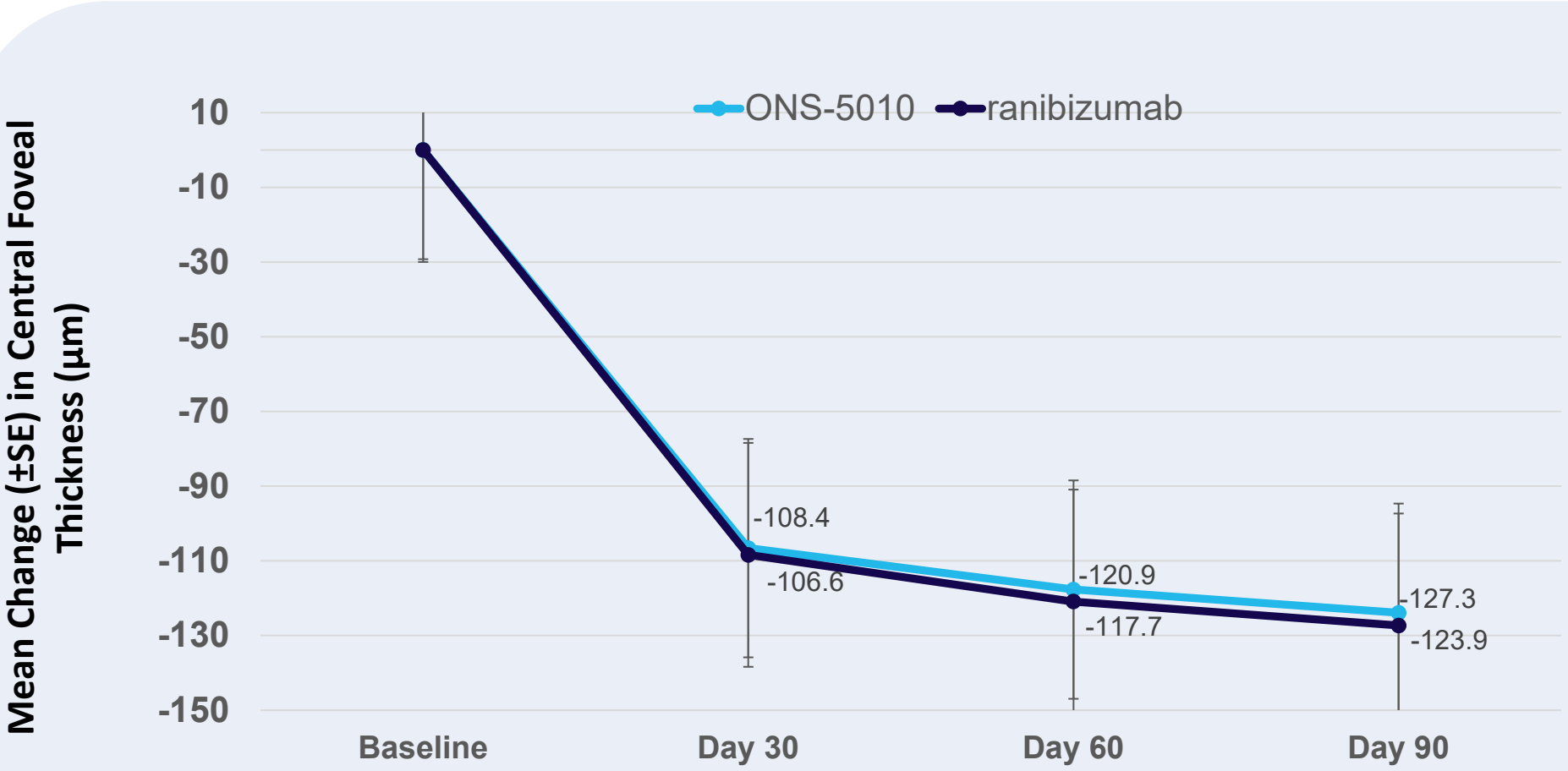
Characteristic	Statistic	ONS-5010 (n=200)	Ranibizumab (n=200)	Overall (n=400)
Female	n (%)	133 (66.5)	115 (57.5)	248 (62.0)
Age in years	median (min, max)	79 (59, 96)	78 (56, 96)	79 (56, 96)
Race				
White	n (%)	194 (97.0)	195 (97.5)	389 (97.3)
Black	n (%)	5 (2.5)	3 (1.5)	8 (2.0)
Asian	n (%)	1 (0.5)	1 (0.5)	2 (0.5)
American Indian/Alaska Native	n (%)	0	1 (0.5)	1 (0.3)
Ethnicity				
Hispanic or Latino	n (%)	13 (6.5)	10 (5.0)	23 (5.8)
Non-Hispanic or Latino	n (%)	187 (93.5)	190 (95.0)	377 (94.3)
Study Eye				
Right Eye	n (%)	94 (47.0)	100 (50.0)	194 (48.5)
Left Eye	n (%)	106 (53.0)	100 (50.0)	206 (51.5)
Baseline BCVA	mean (SD)	58.8 (11.10)	59.9 (10.30)	59.4 (10.71)
Baseline CFT	mean (SD)	389.9 (135.76)	368.3 (114.32)	379.1 (125.04)

Efficacy: Best Corrected Visual Acuity



BCVA: Best Corrected Visual Acuity. SE: standard error.

Efficacy: Central Foveal Thickness



SE: standard error.

Safety Results

Adverse Events	ONS-5010 (n=200)	Ranibizumab (n=200)
≥ 1 Adverse Event n (%)	**91 (45.5)**	**71 (36.0)**
≥ 1 Ocular Adverse Event n (%)	51 (25.5)	47 (23.5)
≥ 1 Non-Ocular Adverse Event n (%)	58 (29.0)	35 (17.5)
≥ 1 Serious Adverse Event n (%)	**9 (4.5)**	**5 (2.5)**
≥ 1 Ocular Serious Adverse Event n (%)	1 (0.5)	0
≥ 1 Non-Ocular Serious Adverse Event n (%)	8 (4.0)	5 (2.5)
Most common Adverse Event in the study eye n (%)		
Conjunctival hemorrhage	5 (2.5)	5 (2.5)

Safety Results: Frequency and Incidence of Ocular AEs ≥ 3 eyes

Characteristic	Statistic	ONS-5010 (n=200)	Ranibizumab (n=200)
≥ 1 Ocular TEAE in Study Eye	**n (%)**	**51 (25.5)**	**47 (23.5)**
Conjunctival hemorrhage	n (%)	5 (2.5)	5 (2.5)
Vitreous detachment	n (%)	4 (2.0)	4 (2.0)
Retinal pigment epithelial tear	n (%)	3 (1.5)	5 (2.5)
Eye pain	n (%)	5 (2.5)	2 (1.0)
Visual acuity reduced	n (%)	5 (2.5)	2 (1.0)
Vitreous floaters	n (%)	4 (2.0)	2 (1.0)
Retinal hemorrhage	n (%)	2 (1.0)	2 (1.0)
Choroidal neovascularization	n (%)	1 (0.5)	3 (1.5)
Subretinal fibrosis	n (%)	2 (1.0)	2 (1.0)
Macular scar	n (%)	2 (1.0)	1 (0.5)
Detachment of retinal pigment epithelium	n (%)	0	3 (1.5)
Dry age-related macular degeneration	n (%)	1 (0.5)	2 (1.0)
Dry eye	n (%)	1 (0.5)	2 (1.0)
Neovascular age-related macular degeneration	n (%)	6 (3.0)	8 (4.0)

No cases of retinal vasculitis

Safety Results: Frequency and Incidence of

Characteristic	Statistic	ONS-5010 (n=200)	Ranibizumab (n=200)
≥ 1 Arteriothrombitic Adverse Event*	**n (%)**	**1 (0.5)**	**1 (0.5)**
≥ 1 Non-ocular Event	**n (%)**	**58 (29.0)**	**35 (17.5)**
Urinary tract infection	n (%)	14 (7.0)	3 (1.5)
Hypertension	n (%)	10 (5.0)	1 (0.5)
COVID-19	n (%)	3 (1.5)	1 (0.5)
Arthralgia	n (%)	2 (1.0)	1 (0.5)
Fall	n (%)	1 (0.5)	2 (1.0)
Tooth infection	n (%)	3 (1.5)	0
Vomiting	n (%)	3 (1.5)	0
Arthritis	n (%)	1 (0.5)	1 (0.5)
Blood pressure increased	n (%)	0	2 (1.0)
Herpes zoster	n (%)	0	2 (1.0)
Nephrolithiasis	n (%)	1 (0.5)	1 (0.5)
Pain in extremity	n (%)	0	2 (1.0)
Palpitations	n (%)	1 (0.5)	1 (0.5)
Skin laceration	n (%)	1 (0.5)	1 (0.5)
Tooth fracture	n (%)	0	2 (1.0)
Upper respiratory tract infection	n (%)	1 (0.5)	1 (0.5)

*ATE's include nonfatal stroke (n=1), nonfatal heart attack (n=1), and death by cardiac related event (n=0)

Summary

Clinically Relevant Outcomes

- ONS-5010 demonstrated clinically meaningful anatomic and functional improvements across the NORSE EIGHT study
  - BCVA was statistically noninferior to ranibizumab at Day 30 and Day 90
  - Change in central foveal thickness was similar in both study arms at all three study timepoints

Safety Findings

- ONS-5010 was generally well-tolerated with ocular adverse event rates comparable to ranibizumab
- No retinal vasculitis reported in either study arm
- Most commonly reported adverse event was conjunctival hemorrhage
- Safety results of NORSE EIGHT are consistent with those previously reported for the NORSE ONE, NORSE TWO, and NORSE THREE clinical trials

NORSE EIGHT will be included in the ONS-5010 BLA resubmission planned for filing in 1Q2025

Thank You