OPT-302 Phase 2b in wet AMD

A multicenter, randomized, double-masked, sham controlled study of intravitreal OPT-302 in combination with ranibizumab, in participants with wet AMD

Data presented by Professor Timothy Jackson PhD., FRCOphth., King's College London
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Contact: Megan Baldwin PhD, CEO and Managing Director, Opthea Limited

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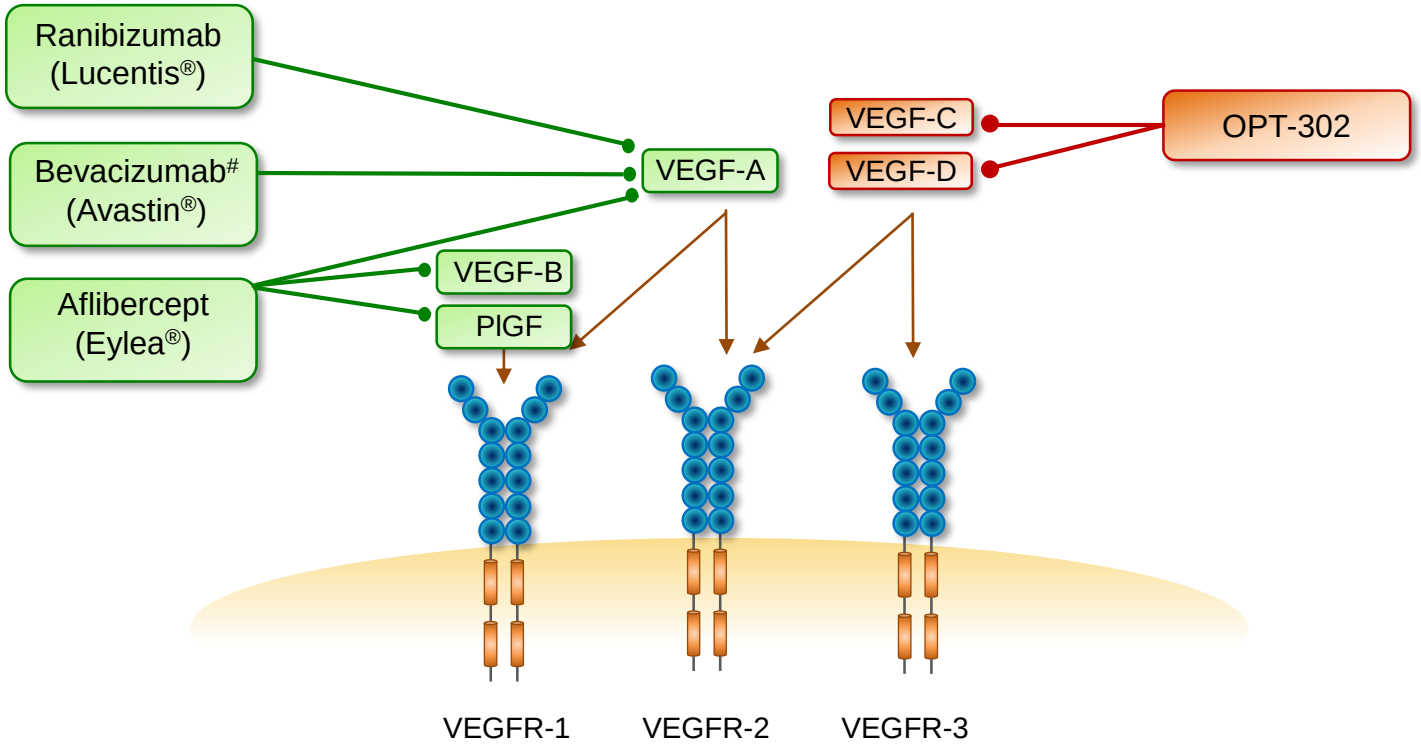
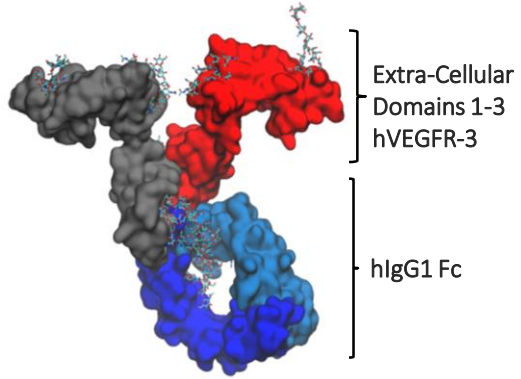
OPT-302 Inhibits VEGF-C and VEGF-D



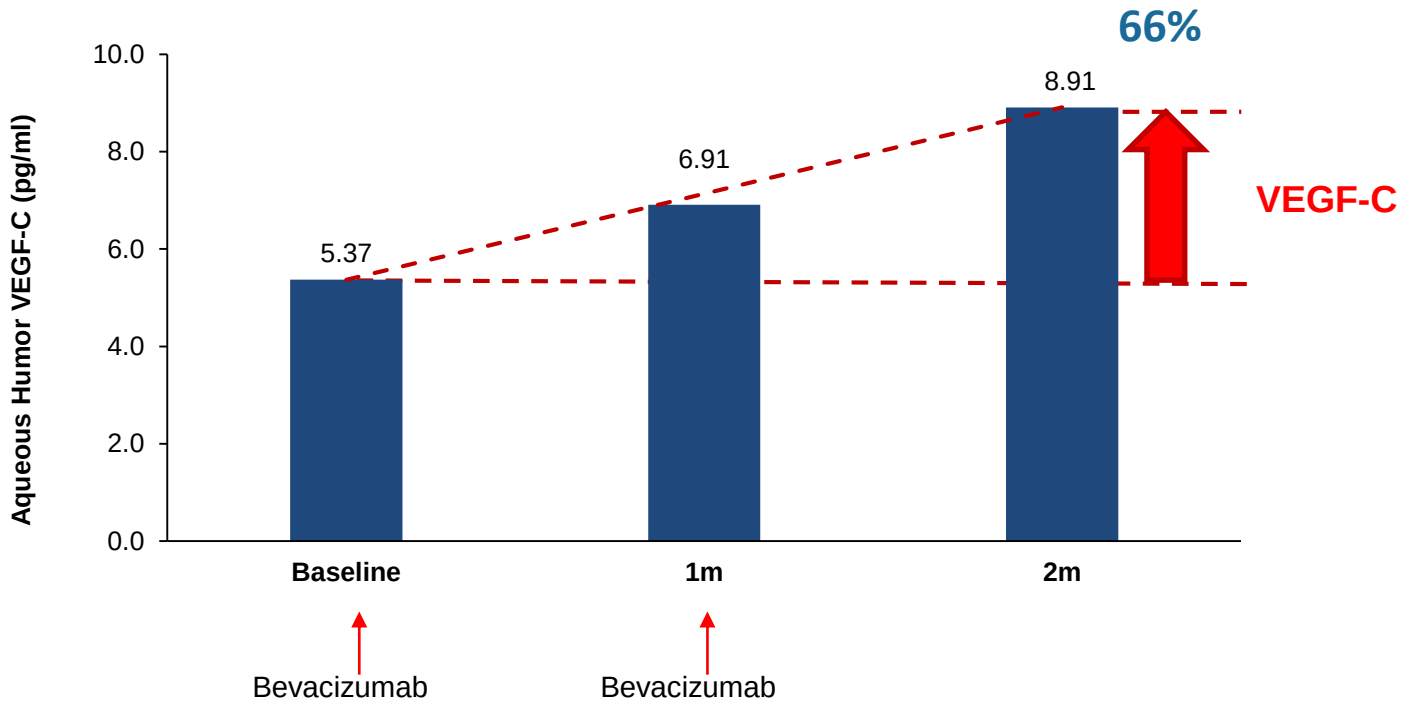


- Potent inhibitor of VEGF-C (~5pM) and VEGF-D (~0.5 nM)
- A 'trap' that blocks VEGF-C and VEGF-D binding to the receptors VEGFR-2 and VEGFR-3

 # Bevacizumab is used 'off-label' for the treatment of nAMD

VEGF-A Inhibition Upregulates VEGF-C/D

Upregulation in Neovascular AMD [1]



[1] *Cabral et al., Bevacizumab injection in patients with neovascular Age-Related Macular Degeneration increases angiogenic biomarkers, Opthalmol Retina, 2(1): 31-37, 2018*

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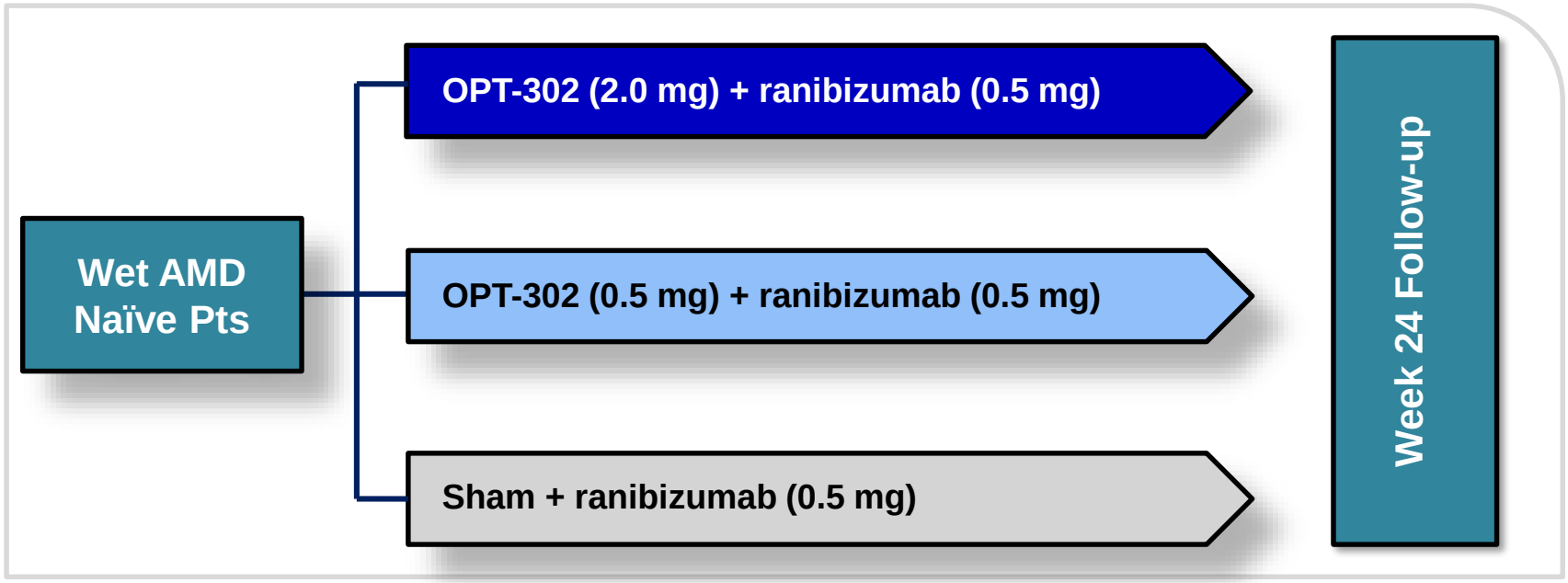
OPT-302-1002 – Study Overview

ClinicalTrials.gov Identifier: NCT03345082

Randomised 1:1:1 to treatment arms : intravitreal dosing every 4 weeks (x 6)



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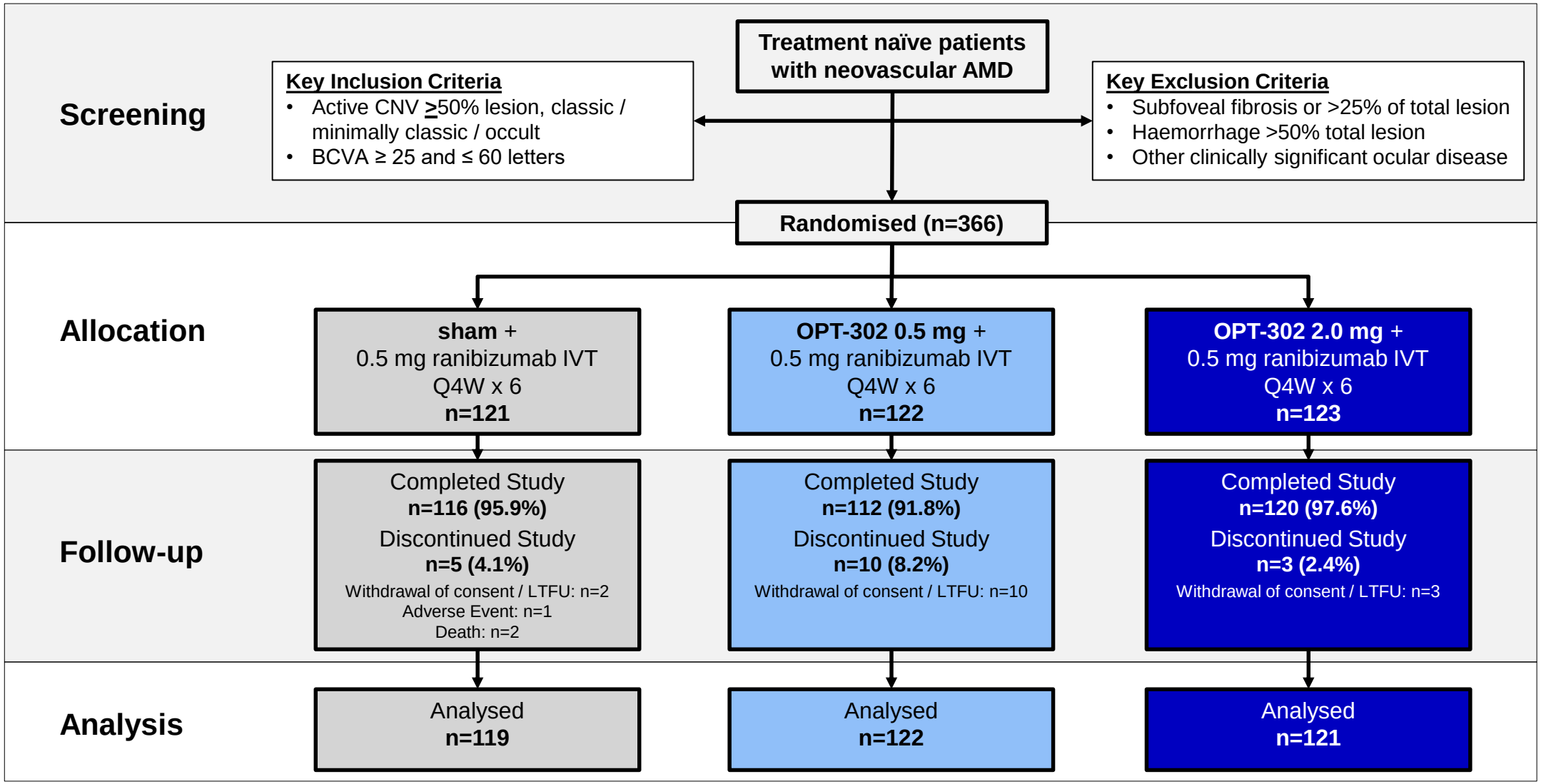
Study Overview



CNV – choroidal neovascularisation; LTFU – lost to follow up

Study Outcome Measures

Primary Outcome:

- Mean change from Baseline in ETDRS best corrected visual acuity at Week 24

Key Secondary Outcomes at Week 24:

- Patients gaining ≥15 or more ETDRS letters
- Patients losing ≥15 or more ETDRS letters
- Change in central subfield thickness (SD-OCT)
- Change in subretinal fluid and intraretinal fluid (SD-OCT)

Key Exploratory Outcomes at Week 24:

- Change in total lesion area and choroidal neovascularisation (CNV) area

Key Safety Outcome:

- Safety and tolerability

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Study Demographics and Baseline Characteristics

Evenly balanced across groups

Demographic / Baseline Disease Characteristic	Sham + ranibizumab N=121	0.5 mg OPT-302 + ranibizumab N=122	2.0 mg OPT-302 + ranibizumab N=123
Mean Age – years ± SD	76.1 ± 9.48	78.8 ± 8.16	77.8 ± 8.82
Sex – n (%)			
Male	48 (39.7%)	49 (40.2%)	45 (36.6%)
Female	73 (60.3%)	73 (59.8%)	78 (63.4%)
Caucasian Race – n (%)	117 (99.2%)	119 (99.2%)	117 (97.5%)
Mean Visual Acuity (BCVA) – letters ± SD	50.7 ± 10.21	51.1 ± 8.96	49.5 ± 10.26
Mean Total Lesion Area - mm^2 ± SD	6.08 ± 3.21	6.48 ± 3.30	6.62 ± 3.39
Lesion type			
Predominantly classic – n (%)	15 (12.4%)	15 (12.3%)	16 (13.0%)
Minimally classic – n (%)	53 (43.8%)	51 (41.8%)	53 (43.1%)
Occult - n (%)	53 (43.8%)	56 (45.9%)	54 (43.9%)
Mean central subfield thickness (CST) - mm ±SD	412.10 ± 110.62	425.18 ± 120.45	414.12 ± 123.25
Sub-retinal fluid (SRF) present – % participants	89.3%	84.4%	87.8%
Intra-retinal cysts present – % participants	57.9%	63.9%	56.1%

Intent-to-Treat (ITT) population; SD: standard deviation; BCVA: Best Corrected Visual Acuity

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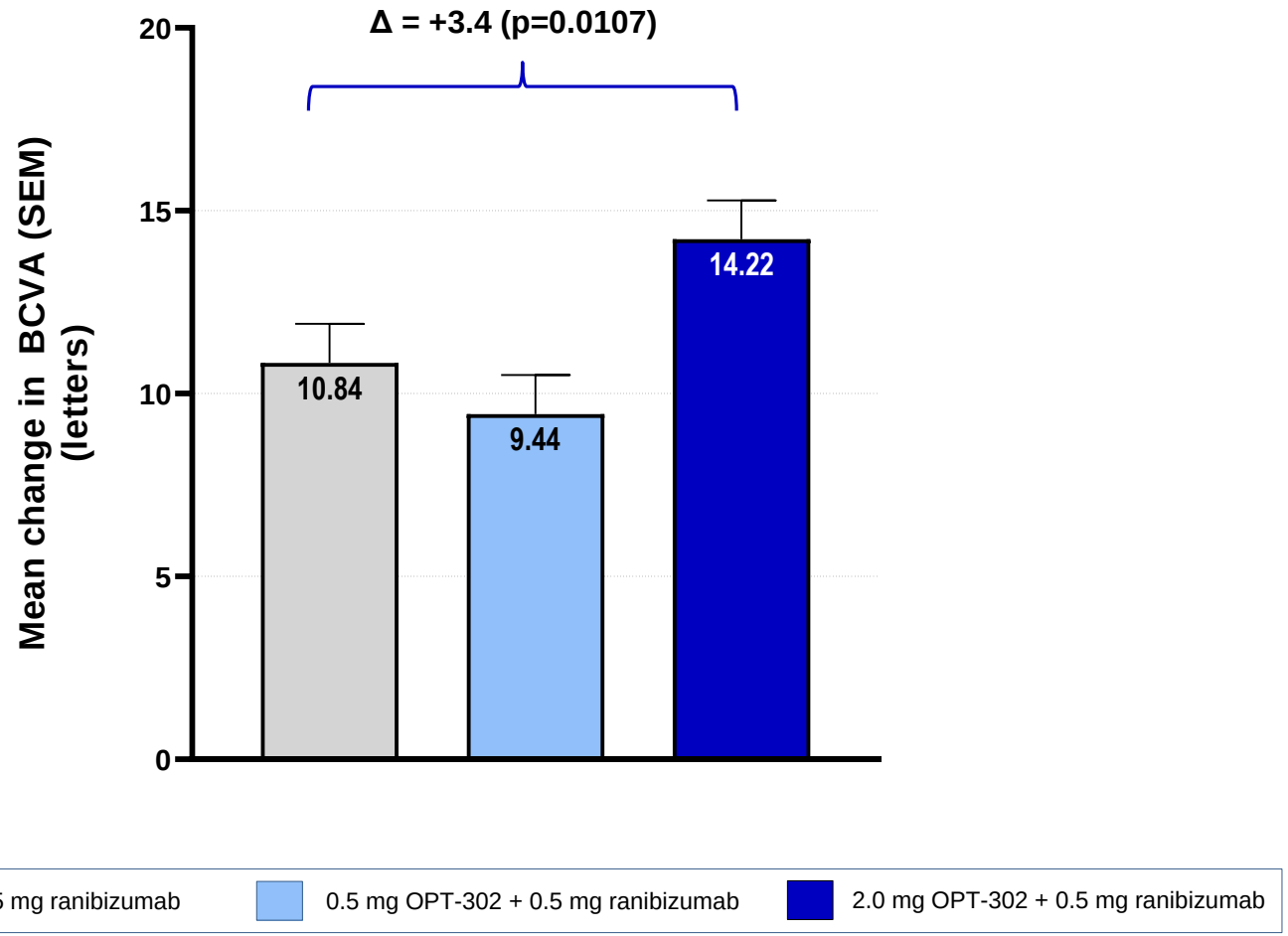
Primary Analysis – Mean Change in BCVA Baseline to Week 24

Primary endpoint achieved

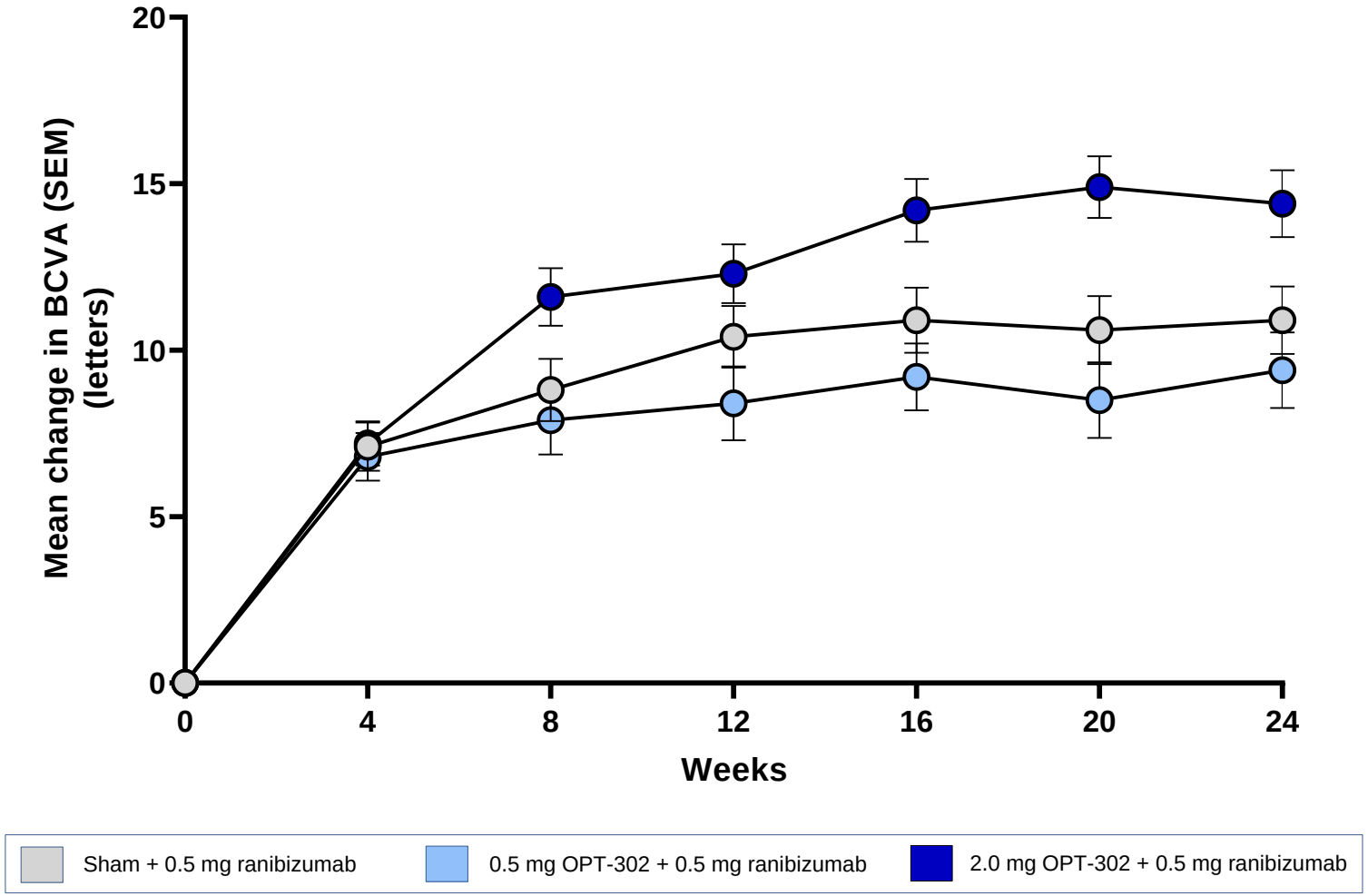
OPT-302 Combination Therapy Demonstrated Superiority in Visual Acuity over Ranibizumab



Modified Intent-to-Treat (mITT) population; BCVA – Best Corrected Visual Acuity;
Graph represents difference in Least Square Means, using Model for Repeated Measures (MRM) analysis, and standard error of the mean (SEM);
Control of Type I error via the Hochberg Procedure

Mean Change in BCVA Over Time

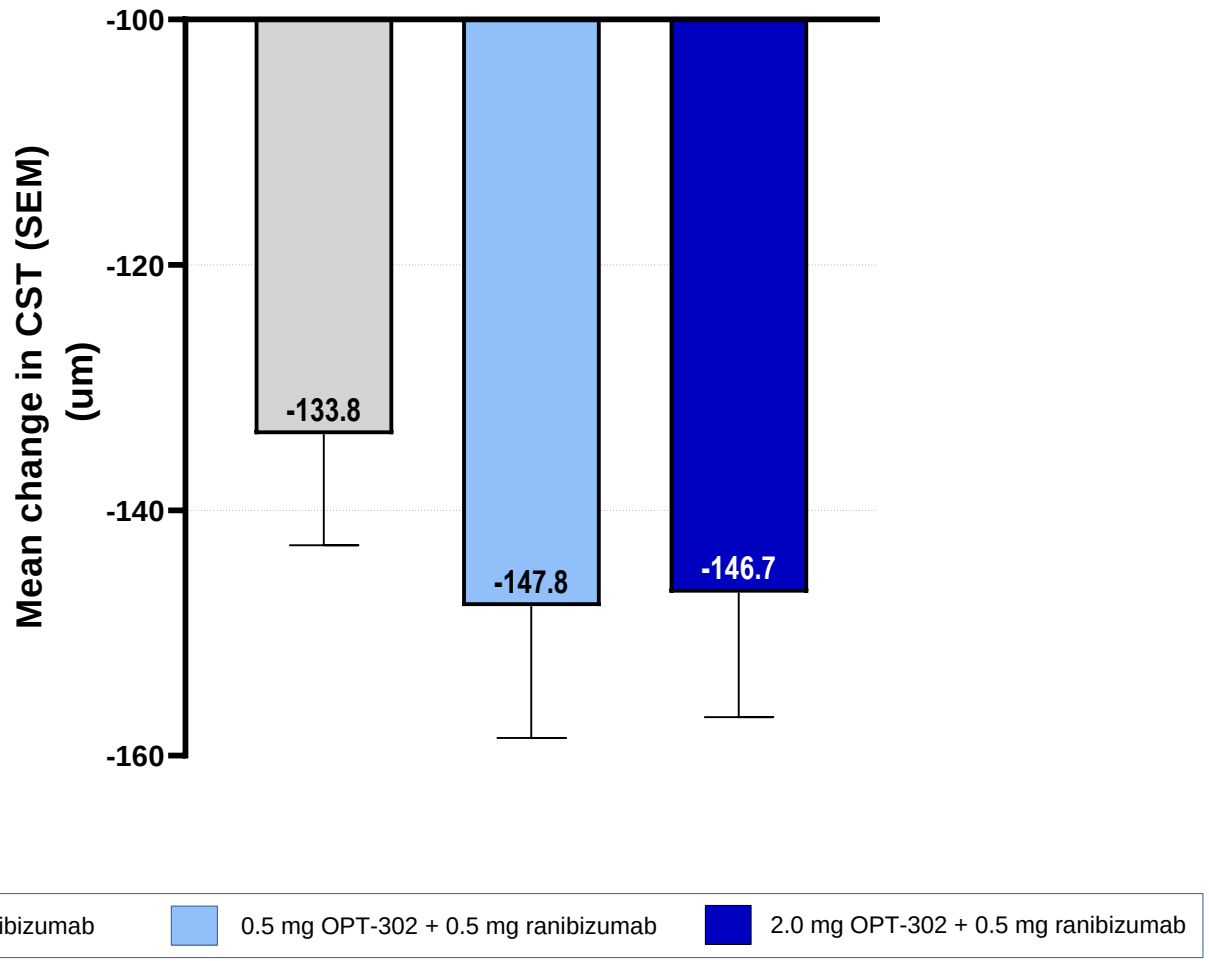
Additive benefit of OPT-302 evident from 8-weeks



mITT; graph represents "as observed" data and SEM

Mean Change in Central Subfield Thickness - Baseline to Week 24

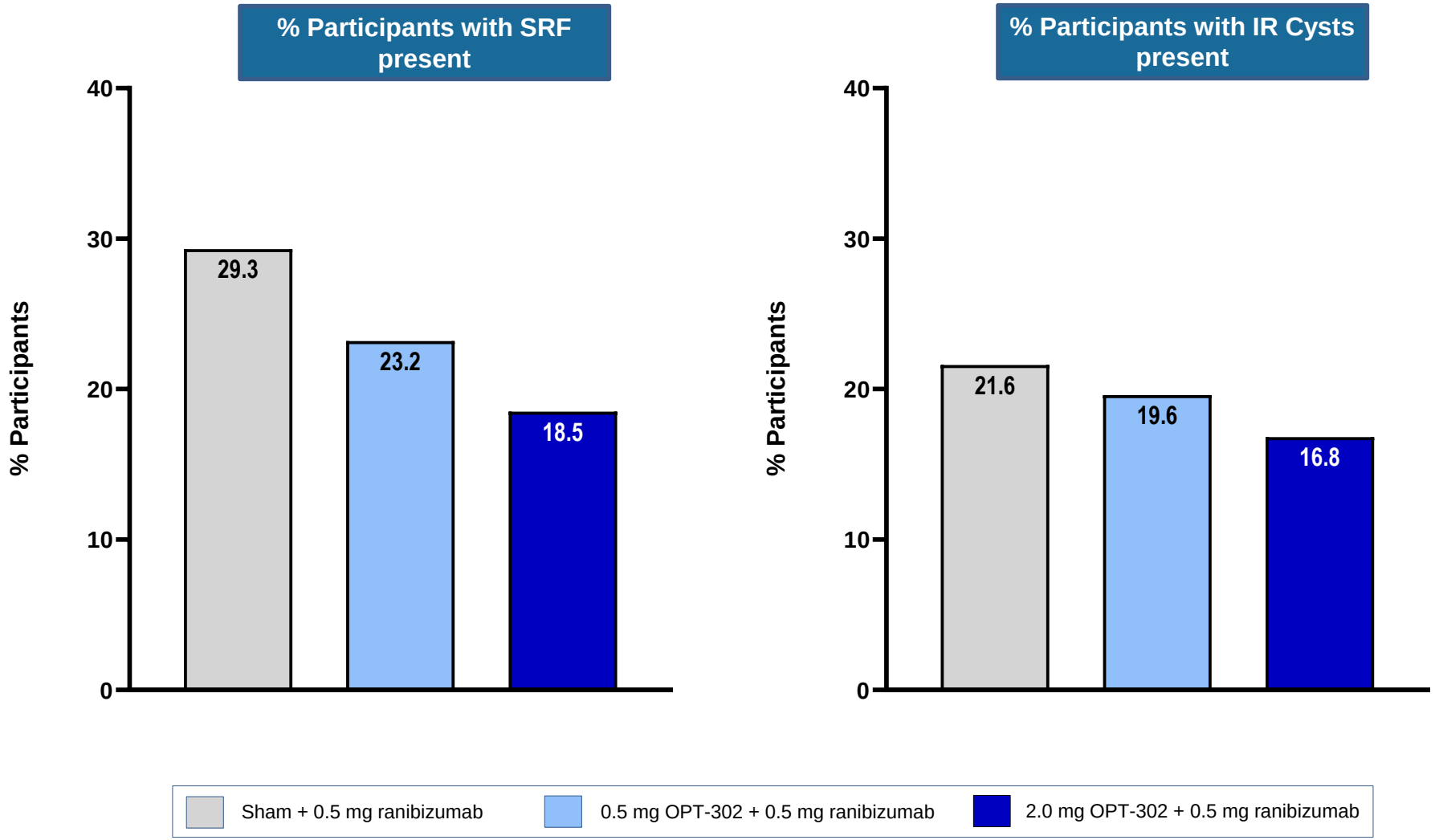
Reductions in CST in OPT-302 combination groups compared to sham + ranibizumab



mITT; as observed; CST – central subfield thickness

Sub-retinal Fluid and Intra-retinal Cysts at Week 24

Fewer participants with retinal fluid present in OPT-302 combination groups compared to sham + ranibizumab



mITT; as observed; SRF – sub-retinal fluid; IR – intra-retinal

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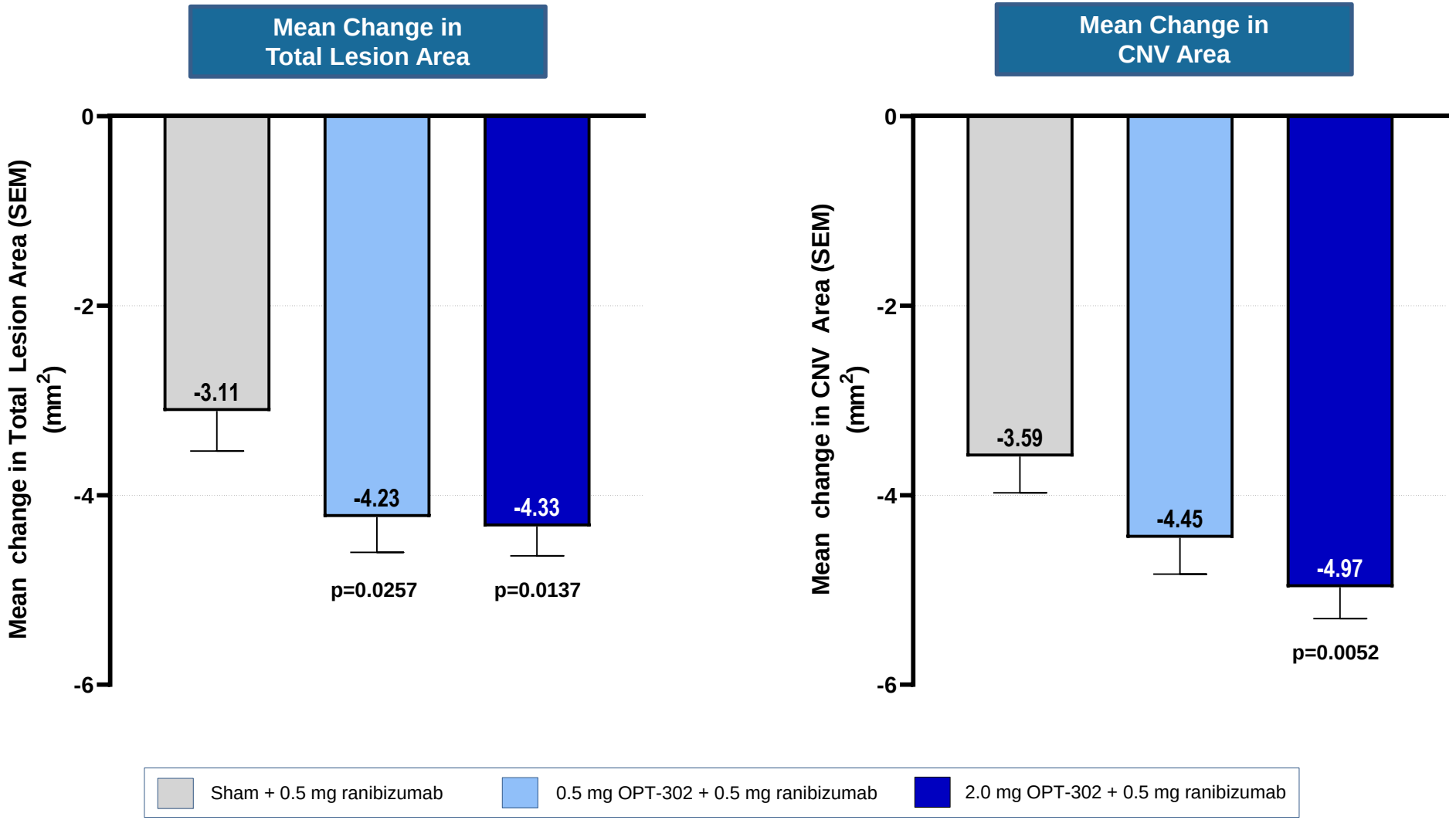
Mean Change in Total Lesion Area and CNV Area – Baseline to Week 24

Greater reduction in Total Lesion and CNV Area in OPT-302 combination groups compared to sham + ranibizumab



mITT; as observed; CNV – choroidal neovascularisation; Difference in Least Square Means

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Safety – Adverse Events (AEs)

N Participants (%)	Sham + ranibizumab N=121	0.5 mg OPT-302 + ranibizumab N=120	2.0 mg OPT-302 + ranibizumab N=124
Treatment emergent AEs	84 (69.4%)	87 (72.5%)	93 (75.0%)
Ocular AEs - Study Eye – related to study product(s)[1]	17 (14.0%)	17 (14.2%)	19 (15.3%)
Ocular AEs - Study Eye – Severe[2]	1 (0.8%)	2 (1.7%)	1 (0.8%)
Serious AEs	10 (8.3%)	16 (13.3%)	7 (5.6%)
Ocular SAEs in Study Eye	0 (0.0%)	2[3] (1.7%)	0 (0.0%)
Intraocular inflammation[4] – Study Eye	0 (0.0%)	2[3] (1.7%)	1[5] (0.8%)
AEs leading to study IP discontinuation only	2 (1.7%)	3 (2.5%)	0 (0.0%)
AEs leading to study discontinuation	1[6] (0.8%)	0 (0.0%)	0 (0.0%)
Any APTC event	0 (0.0%)	1[7] (0.8%)	0 (0.0%)
Deaths	2[8] (1.7%)	0 (0.0%)	0 (0.0%)

Safety population analysed according to medication received

[1] Assessed by investigator to be "possibly related", "probably related" or "definitely related" to administration of study drug(s)

[2] Assessed by Investigator to be National Institutes of Health (NIH) Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or above, or, if CTCAE grade is unavailable, an AE assessed as "causing an inability to perform normal daily activities"

[3] SAE of endophthalmitis, with AEs of hypopyon and anterior chamber cell (n=1), SAE of vitritis (n=1)

[4] AEs considered to be indicative of intraocular inflammation, defined prior to database lock as: Endophthalmitis, iritis, vitritis, iridocyclitis, uveitis, hypopyon, viral iritis, or anterior chamber inflammation

[5] Anterior chamber cell (trace 1-4 cells)

[6] Squamous cell carcinoma of the lung diagnosed shortly after Baseline visit

[7] Non-fatal myocardial infarction

[8] Pneumonia (n=1), infective endocarditis (n=1)

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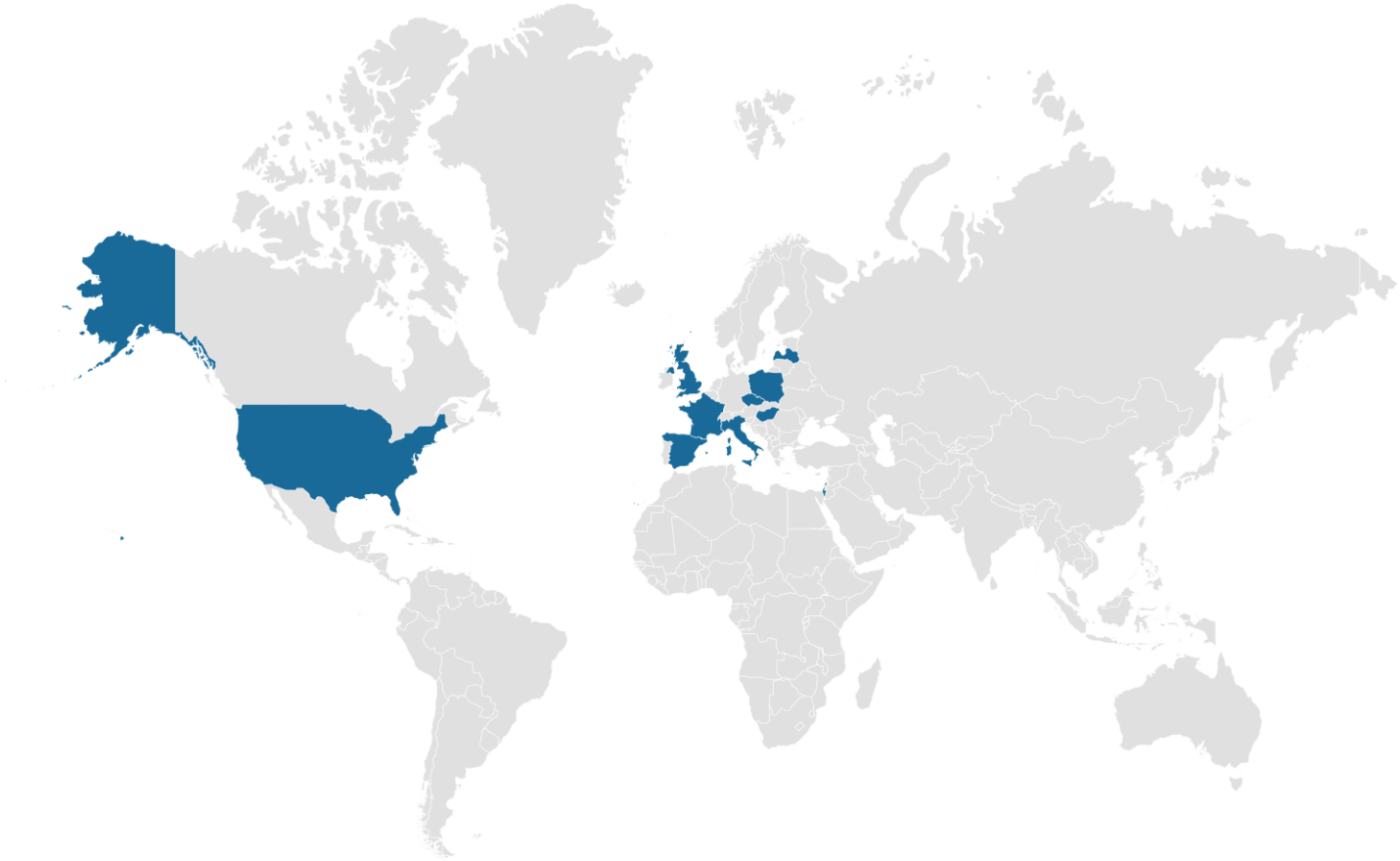
Thank you to all study participants and over 100 sites across 10 countries



Czech Republic – 3 sites
France – 6 sites
Hungary – 5 sites
Italy – 5 sites
Israel – 8 sites
Latvia – 4 sites
Poland – 7 sites
Spain – 8 sites
United Kingdom – 7sites
United States – 56 sites

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Conclusions

- **Phase 2b trial met primary endpoint**
  - OPT-302 (2.0 mg) combination therapy demonstrated superiority in visual acuity over ranibizumab + sham
  - Vision gain of 3.4 letters
  - Statistically significant (p=0.0107)
  - High ranibizumab control arm

- **Secondary outcomes were supportive of the primary endpoint:**
  - **Vision**
    - More patients gained ≥ 15 letters of vision
    - Fewer patients lost ≥ 15 letters of vision
  - **Retinal anatomical improvements**
    - Reductions in CST, subretinal and intraretinal fluid
    - Greater decreases in Total Lesion Area and CNV Area

- **Favourable safety profile similar to ranibizumab alone**

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Megan Baldwin
CEO & Managing Director

T +61 (3) 9826 0399
E megan.baldwin@opthea.com

Suite 0403, Level 4,
650 Chapel Street,
South Yarra 3141 Victoria Australia
www.opthea.com