Durability of Suprachoroidal Triamcinolone Acetonide in Combination with Aflibercept in the Management of Retinal Vein Occlusion: 9-Month Analysis of the *TANZANITE* Phase 2 Trial and Extension Study

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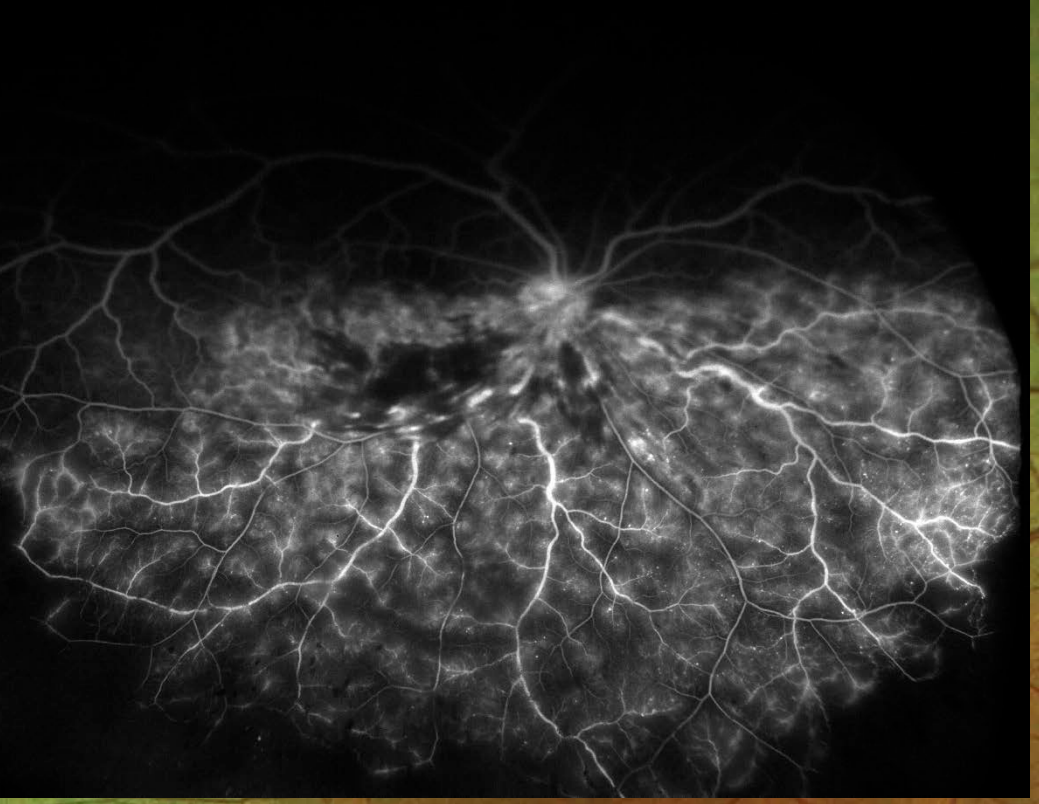
Disclosures

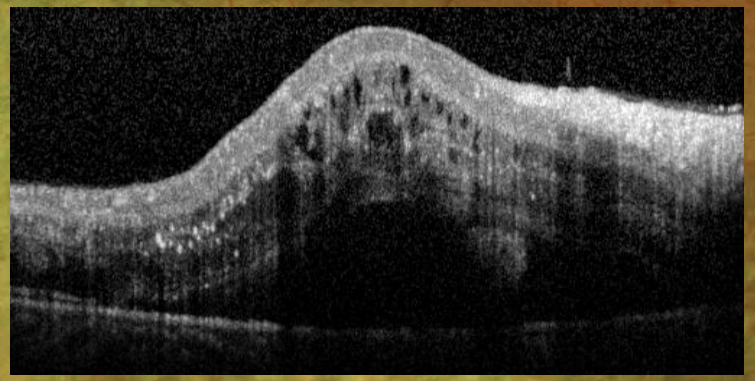
- Financial
  - Consultant - Allergan, Alimera, Bayer, Clearside Biomedical, DORC, Genentech, ONL Therapeutics, Regeneron
  - Speaker - Allergan, Regeneron
  - Research Support – Acucela, Alcon/Novartis, Alimera, Allergan, Apellis, Clearside Biomedical, DORC, DRCR.Net, Genentech/Roche, Iconic, Ophthotech, Regeneron/Bayer, Thrombogenics, Tyrogenex

- Human Subjects
  - This study is Institutional Review Board approved

Retinal Venous Occlusive Disease

Prevalence 1.5% > 75 years

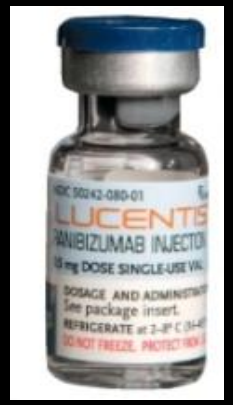




FDA-Approved: ME Secondary to RVO

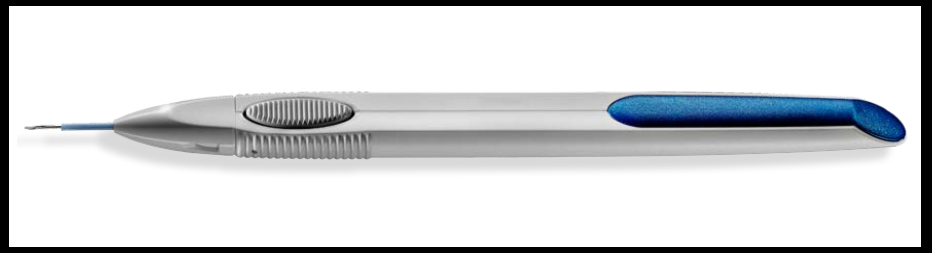
Block VEGF

Ranibizumab



Aflibercept

Dexamethasone



FDA-Approved: ME Secondary to RVO

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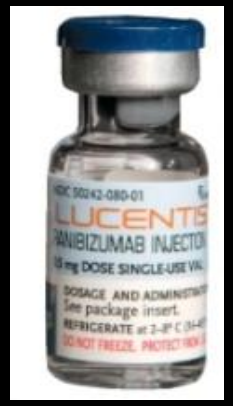
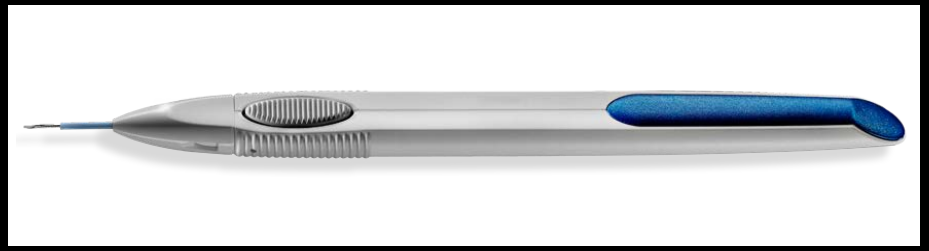


Aflibercept

Dexamethasone



Corticosteroids

Affect a multitude of transcriptional cascades

Inflammation

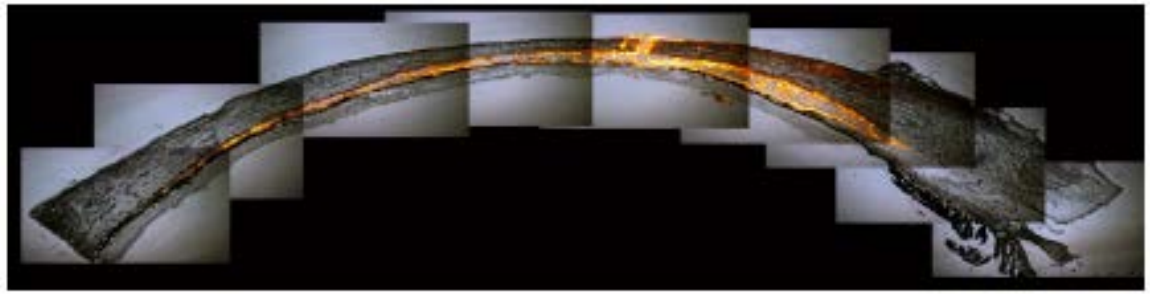
Vascular leakage

Angiogenesis

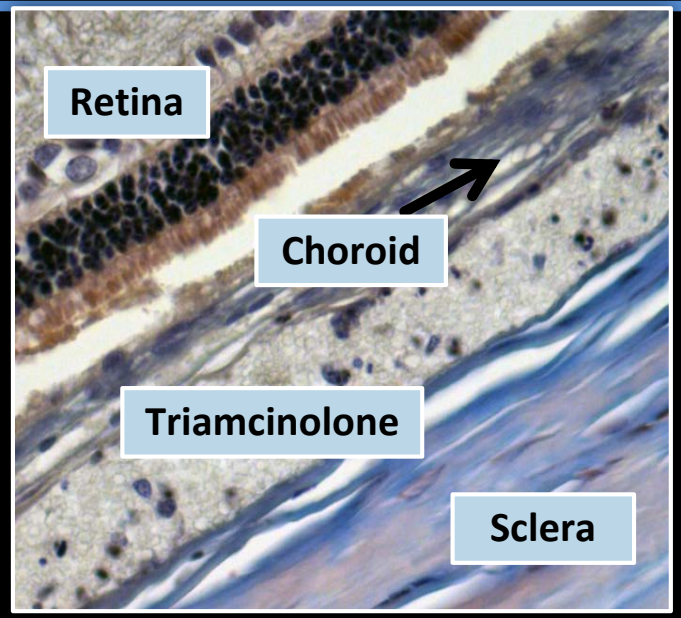
Suprachoroidal Delivery of Corticosteroids

- Maximize drug levels in retina
- Minimize drug levels in AC
- Potential to
  - Reduce cataract acceleration
  - Reduce incidence of increased IOP

Fluorescent particles s/p injection in a pig eye



Triamcinolone acetonide s/p injection in a rabbit eye

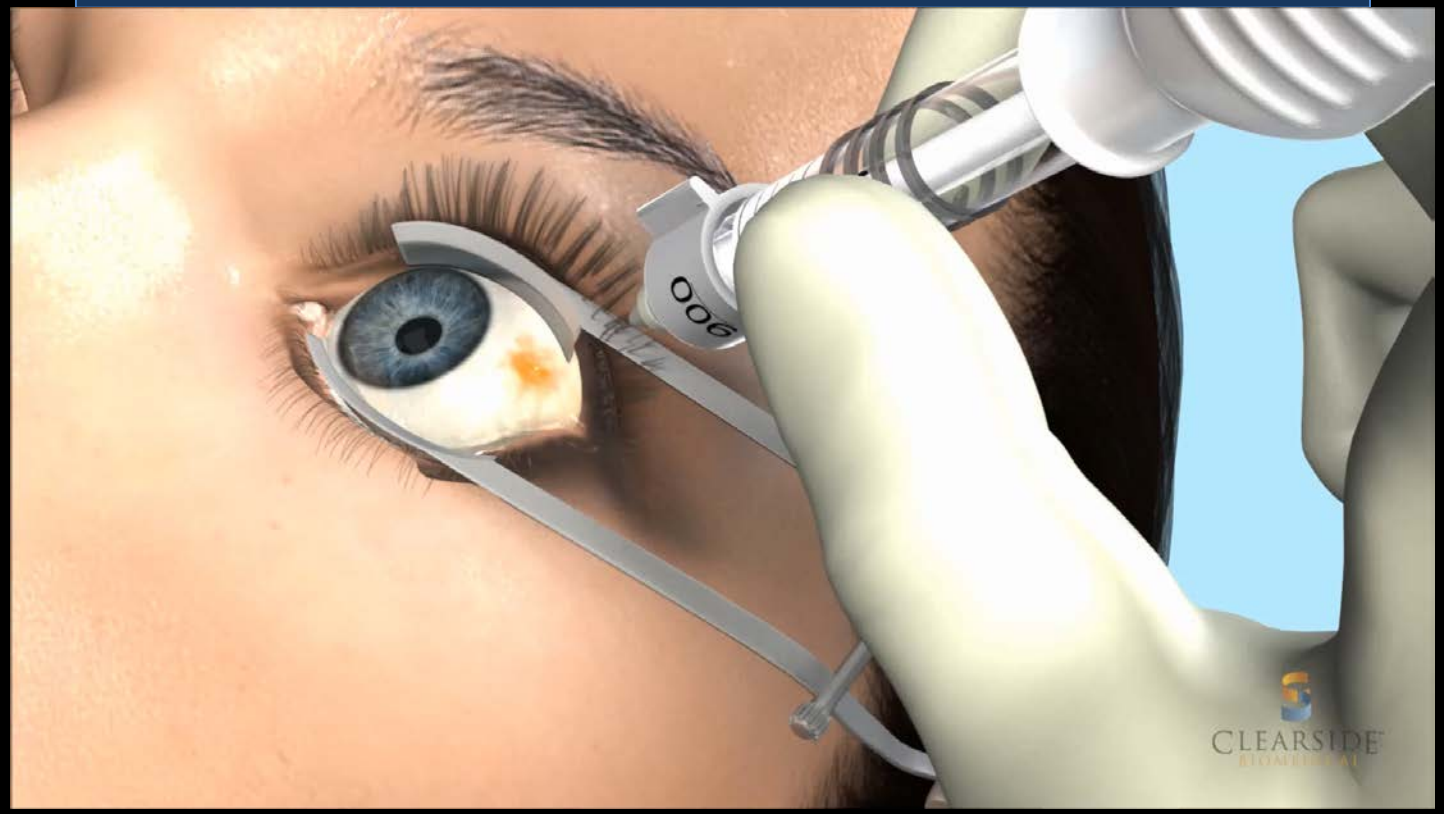


Olsen *AJO* 2006
Patel *IOVS* 2012

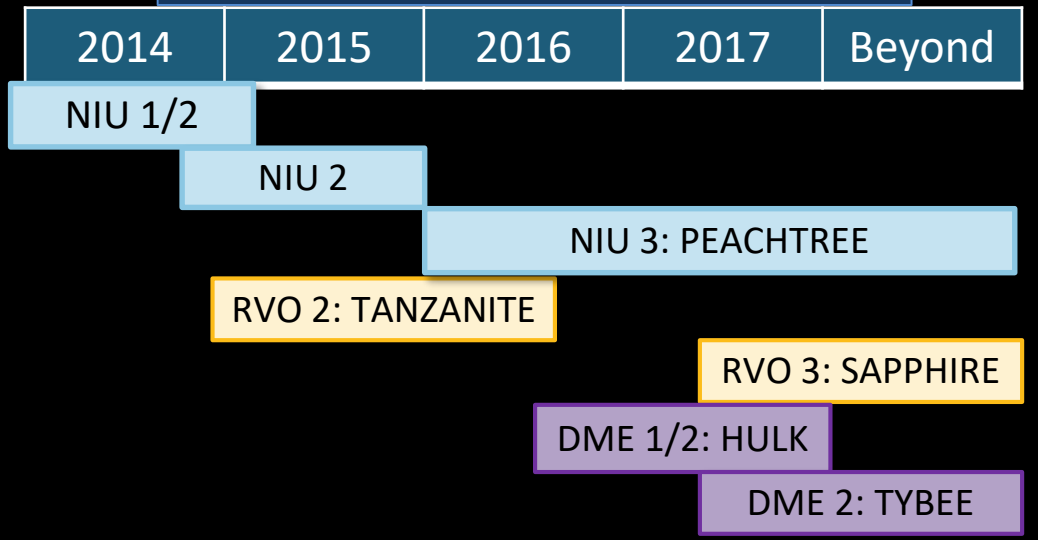
Microneedle

Specifically for Suprachoroidal Delivery of Preservative Free Triamcinolone Acetonide (CLS-TA)

Illustration of CLS-TA Suprachoroidal Delivery



Ongoing Clinical Program

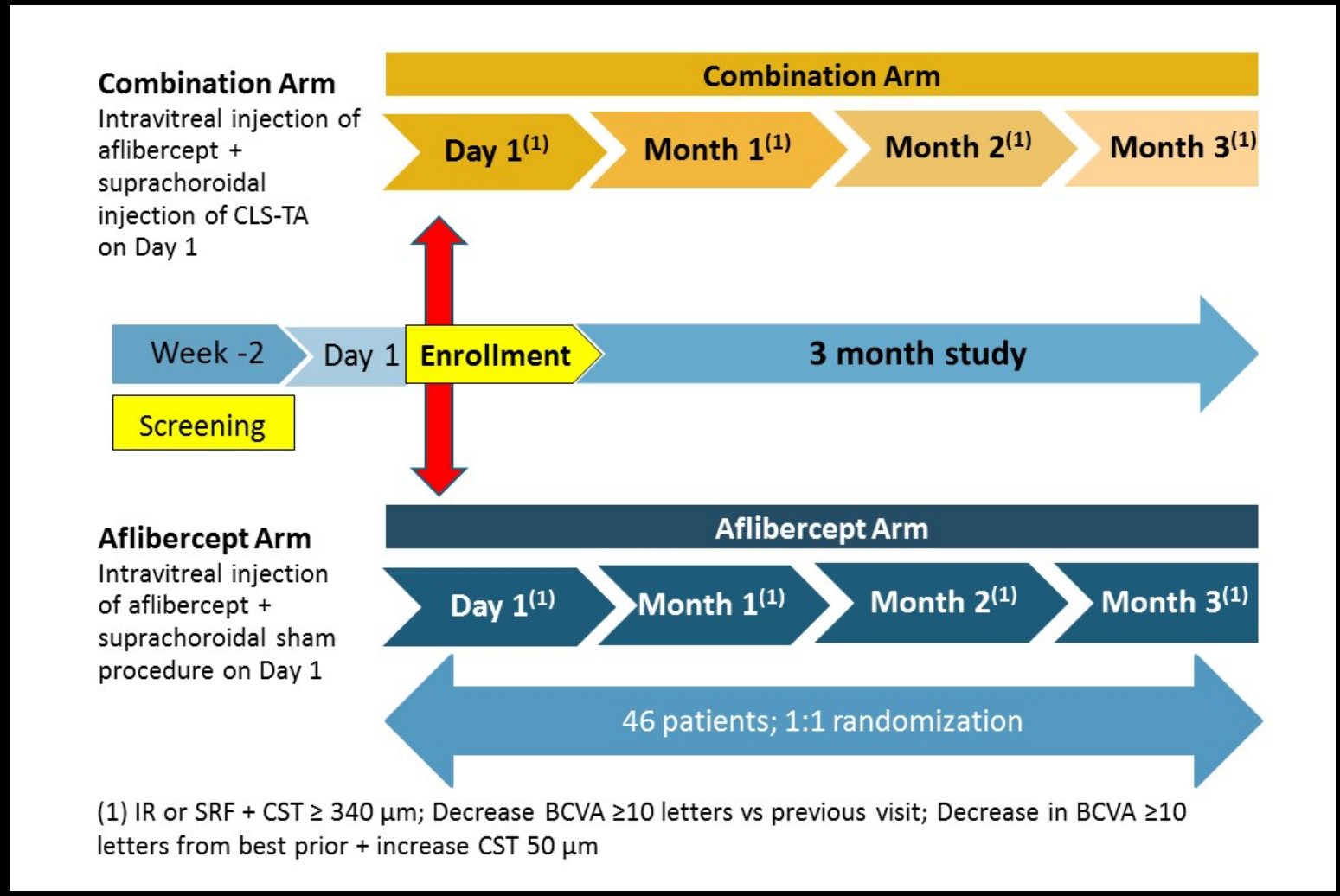


Goldstein *TVST* 2016

CLS-TA: Non-preserved, terminally sterilized, aqueous suspension of triamcinolone acetonide administered as a single injection of 4 mg in 0.1mL

TANZANITE
Phase 2

- 46 Patients
  - CST ≥ 310 µm
  - 20/40-20/400



- Months 1, 2 & 3:

  Determine eligibility for re-treatment
  - IR or SRF + CST ≥ 340 µm
  - Decrease BCVA ≥10 letters vs previous visit
  - Decrease BCVA ≥10 letters from best prior + increase CST 50 µm

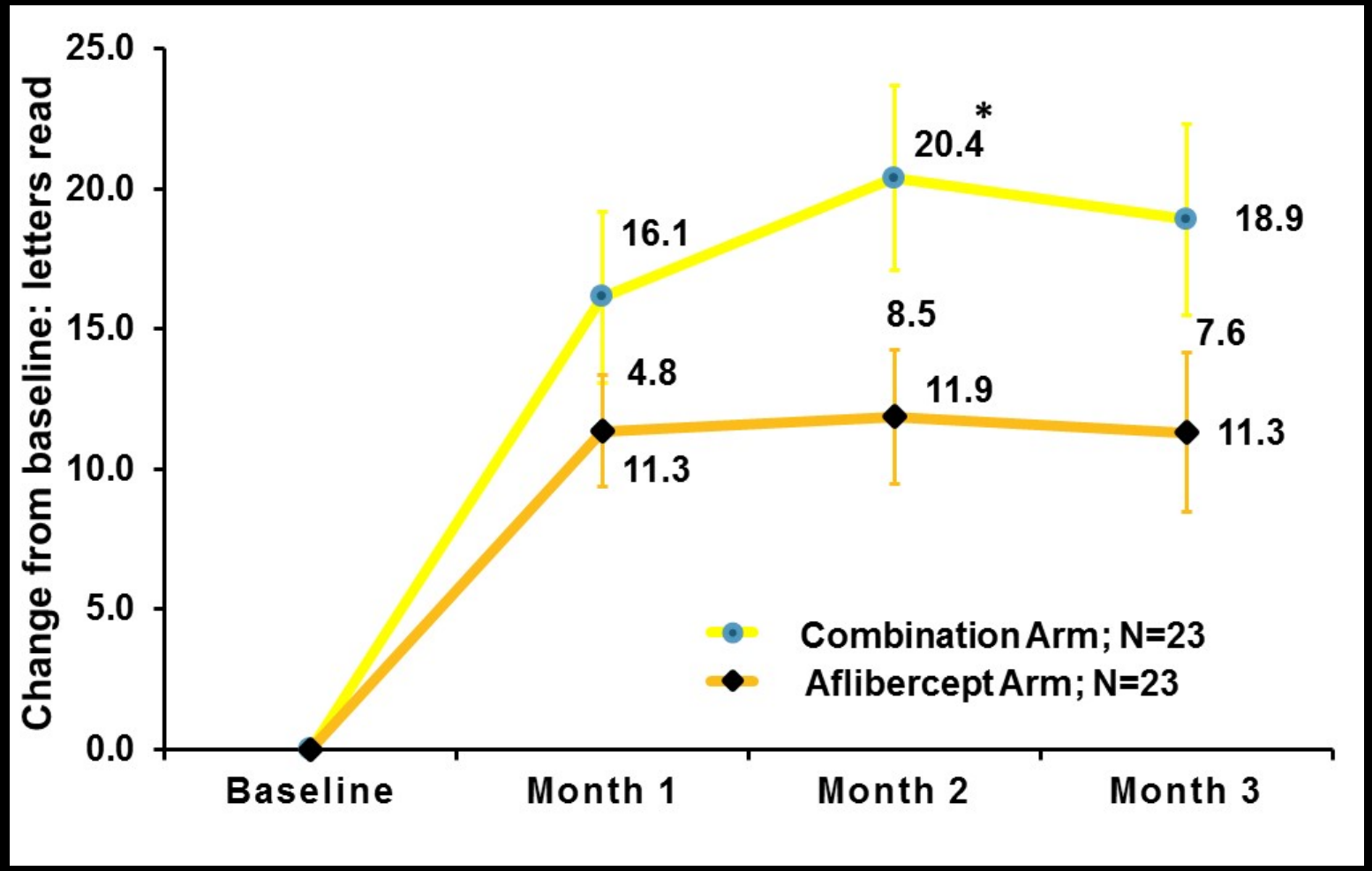
TANZANITE: *Endpoints*

- **Primary**
  - Number of protocol determined aflibercept retreatments through Month 3
- **Secondary**
  - Mean improvements in best corrected visual acuity at Months 1, 2 and 3
  - Mean reductions in macular edema at Months 1, 2 and 3
- **Safety**
  - Incidence of treatment emergent adverse events and serious adverse events
  - Incidence of changes in safety parameters including: IOP, slit lamp bio-microscopy, indirect ophthalmoscopy, imaging parameters and vital signs

TANZANITE: *Change in Mean BCVA*

VA gains greater in the combination arm

(CLS-TA + aflibercept) compared to the monotherapy arm (aflibercept)

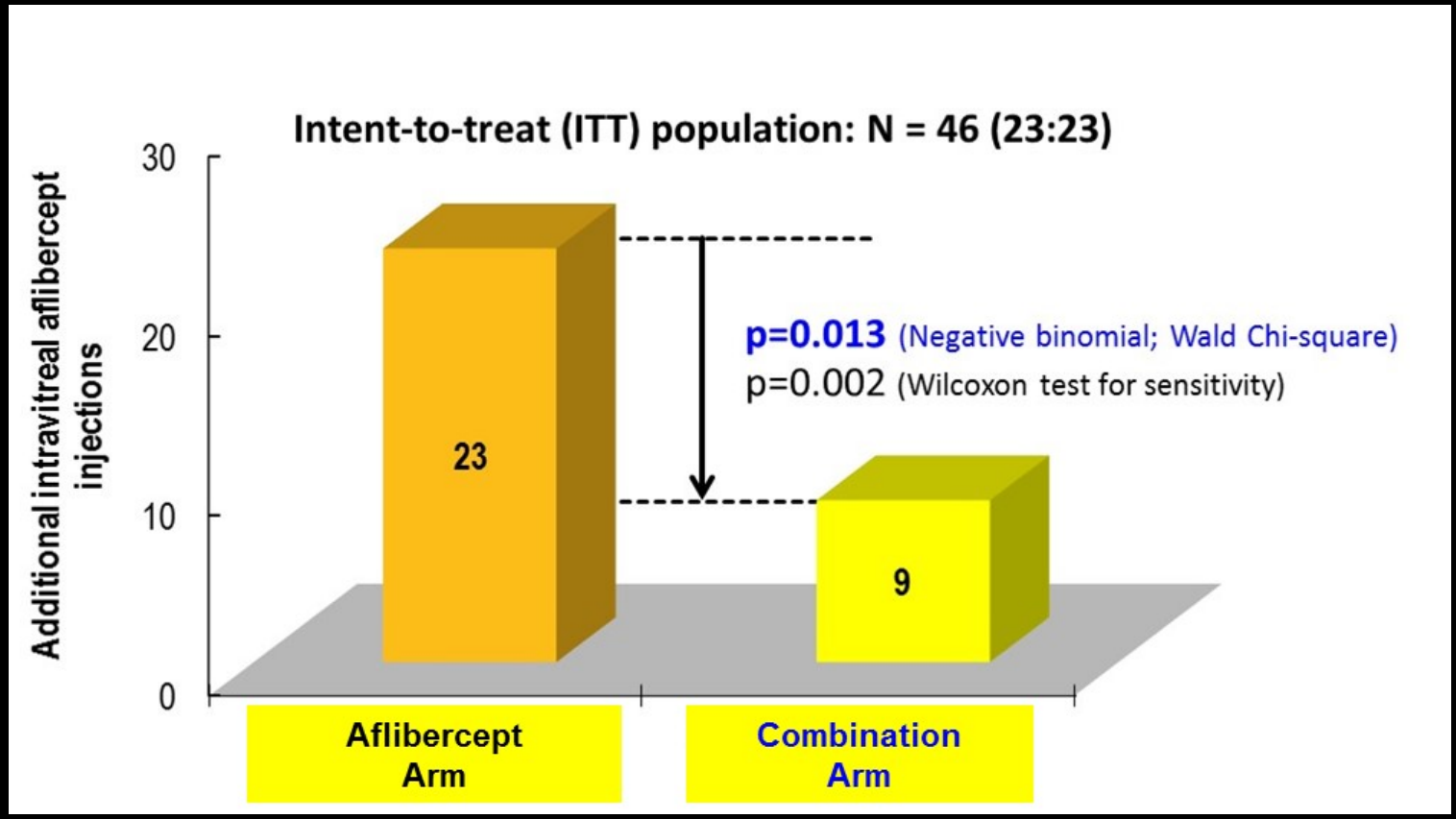


Baseline: 49 ETDRS letters in each arm

Bars are standard error of the mean; * only month 2 showed $p<0.05$

TANZANITE Primary Endpoint

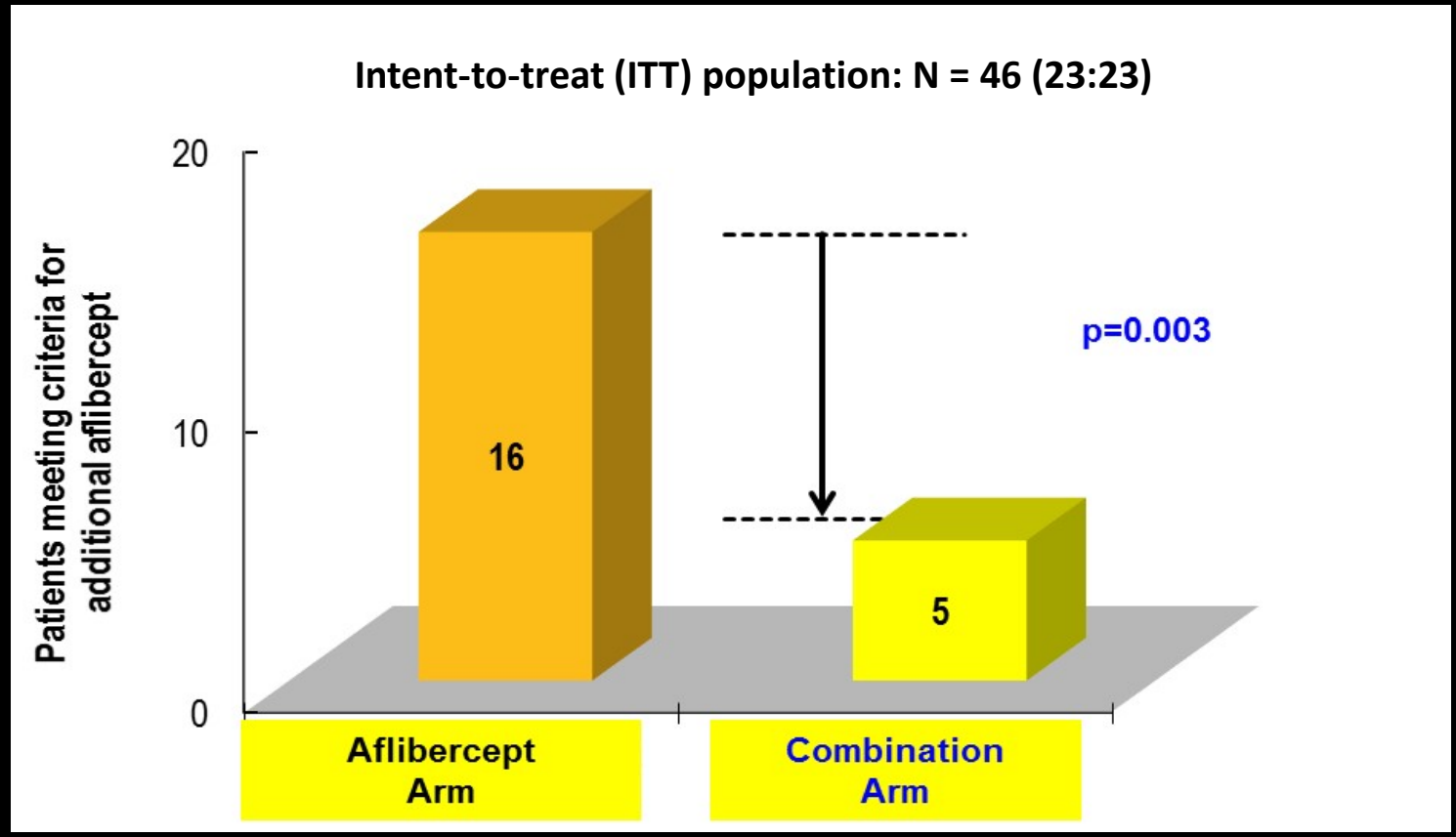
Number of Aflibercept Retreatments



14 fewer aflibercept retreatments in combination arm vs monotherapy arm

61% reduction in the requirement for additional intravitreal aflibercept injections

TANZANITE: *Retreatment by Subjects*



Did not meet criteria for aflibercept retreatment

78% (18/23) in combination arm

30% (7/23) in the control

TANZANITE Extension Study
CLS 1003-202

- Non-interventional & retrospective
- Assess the durability of suprachoroidal CLS-TA in combination with intravitreal aflibercept following completion of TANZANITE

TANZANITE Extension Study
Eligibility and Methods

- Patients who completed TANZANITE & did not receive re-treatment during TANZANITE
- Patients managed according to treating physician's discretion without a prospective protocol
- Records were obtained retrospectively
- **Main efficacy outcome: time to first RVO re-treatment**
- Other outcomes: VA, CRT & Safety assessments

TANZANITE Extension
Enrollment & Re-Treatment

97% (31/32) eligible patients captured in Extension Study.
Mean follow-up time: 247 days (range 1 – 587 days)

Monotherapy (n=11)

6 (55%) re-treated

- 4: aflibercept
- 1: bevacizumab
- 1: unknown agent

Combination (n=20)

3 (15%) re-treated

- 2: aflibercept
- 1: bevacizumab

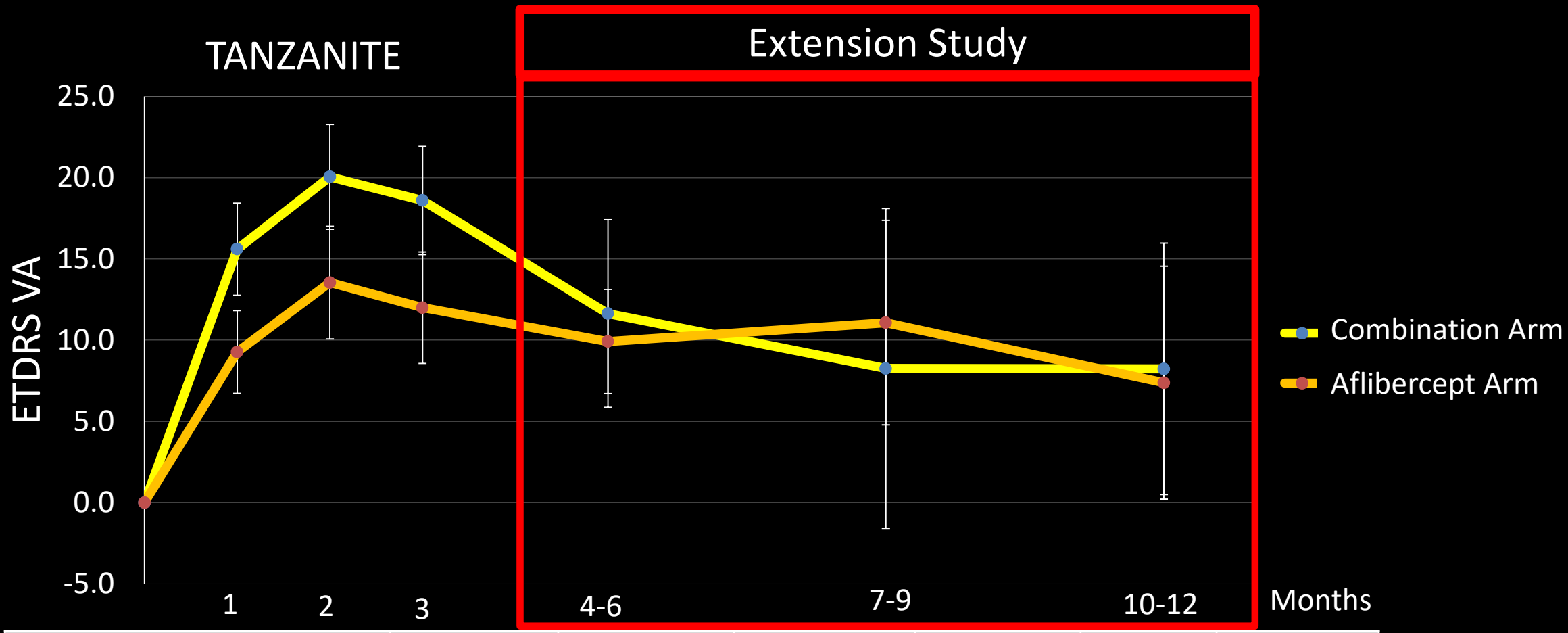
Combination = CLS-TA + aflibercept. Monotherapy = aflibercept

TANZANITE + Extension
Time To and Need for First Re-Treatment

- Mean time to first re-treatment among patients (n=25) who received retreatment
  - Combination — 108 days (26%; n=6)
  - Monotherapy — 68 days (83%; n=21)
- Greater proportion of combination patients never received re-treatment
  - Combination — 74% (n=17/23)
  - Monotherapy — 17% (n=4/23)

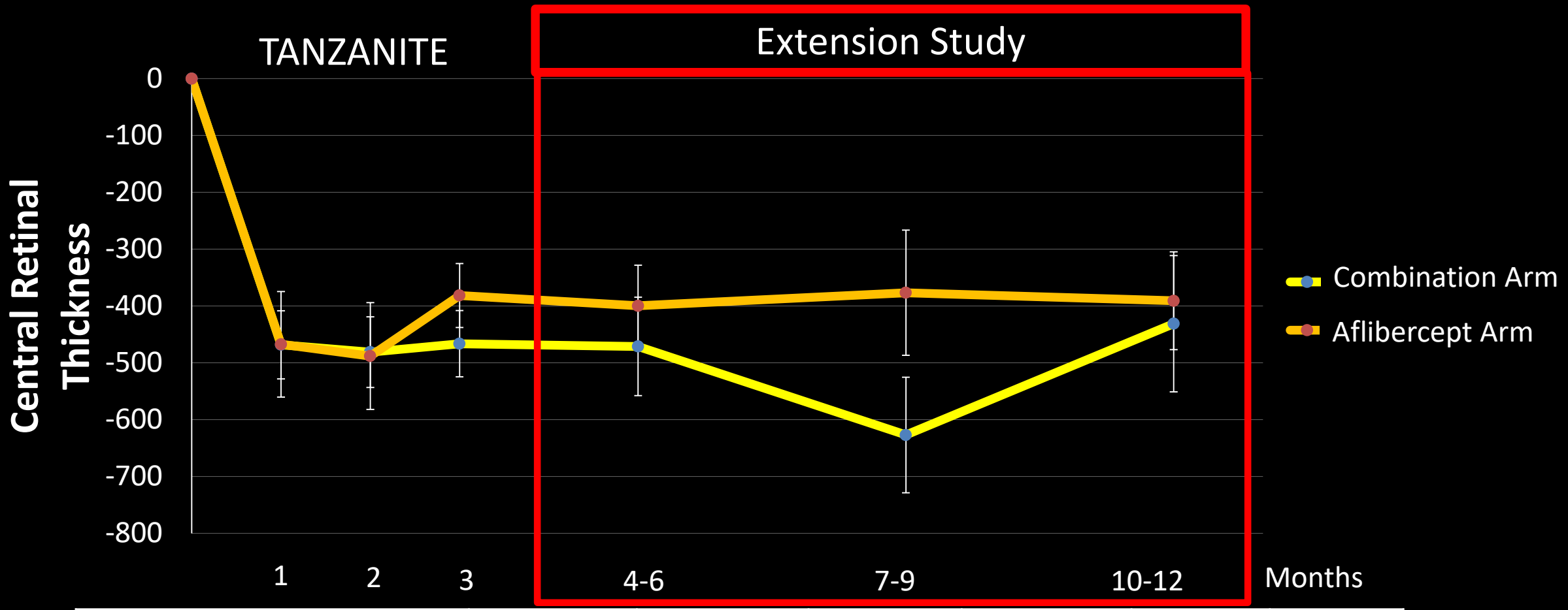
Combination = CLS-TA + aflibercept. Monotherapy = aflibercept

Change in Visual Acuity



Months	1	2	3	4-6	7-9	10-12
Combination Arm (SEM)	15.6 (2.8)	20.1 (3.2)	18.6 (3.3)	11.6 (5.8)	8.3 (9.8)	8.2 (7.7)
n	20	20	20	13	9	9
Aflibercept Arm (SEM)	9.3 (2.5)	13.5 (3.5)	12.0 (3.4)	9.9 (3.2)	11.1 (6.3)	7.4 (7.2)
n	11	11	11	9	7	7

Change in CRT



Months	1	2	3	4-6	7-9	10-12
Combination Arm (SEM)	-468 (60)	-481 (62)	-466 (58)	-471 (87)	-627 (102)	-431 (120)
n	20	20	20	12	9	7
Aflibercept Arm (SEM)	-467 (93)	-488 (94)	-381 (56)	-400 (71)	-377 (110)	-391 (86)
n	11	11	11	9	7	7

TANZANITE Safety: Ocular Adverse Events

	Aflibercept N=23 n (%)	Combination N=23 n (%)	Total N=46 n (%)
Total # of adverse events	12	28	40
Cataract	0	1 (4.3)	1 (2.2)
AC Inflammation	0	1 (4.3)	1 (5)
Conjunctival hemorrhage	1 (4.3)	2 (8.7)	3 (6.5)
Conjunctival hyperemia	1 (4.3)	0	1 (2.2)
Corneal edema	0	1 (4.3)	1 (2.2)
Foreign body sensation	0	1 (4.3)	1 (2.2)
Eye pain	1 (4.3)	8 (34.8)	19 (19.6)
Lacrimation increased	0	1 (4.3)	1 (2.2)
Macular fibrosis	1 (4.3)	0	1 (2.2)
Ocular discomfort	2 (8.7)	0	2 (4.3)
Ocular hypertension	0	2 (8.7)	1 (5)
Optic disc vascular disorder	1 (4.3)	0	1 (2.2)
Optic nerve disorder	0	1 (4.3)	1 (2.2)
Punctate keratitis	0	1 (4.3)	1 (2.2)
Retinal degeneration	1 (4.3)	0	1 (2.2)
Retinal hemorrhage	0	1 (4.3)	1 (2.2)
Vision blurred	1 (4.3)	0	1 (2.2)
Visual acuity reduced	2 (8.7)	0	2 (4.3)
Vitreous detachment	0	1 (4.3)	1 (2.2)
Vitreous floaters	0	1 (4.3)	1 (2.2)
IOP increased	0	2 (8.7)	2 (4.3)

TANZANITE + Extension Study
Conclusions

- The combination of suprachoroidal preservative free triamcinolone acetonide (CLS-TA) with intravitreal aflibercept may increase the durability of treatment effect when managing eyes with ME secondary to RVO

- Additional Trials of CLS-TA in Retinal Vascular Diseases Ongoing
  - RVO
    - **SAPPHIRE** Phase III
  - DME
    - **HULK** Phase I/II
    - **TYBEE** Phase II