

# A Root Cause Analysis of Surgery-Related Adverse Events With Revakinagene Taroretcel-Iwey in Macular Telangiectasia Type 2 Clinical Trials

W. Lloyd Clark,<sup>1</sup> Roger A. Goldberg,<sup>2</sup> John S. Pollack,<sup>3\*</sup> Thomas M. Aaberg, Jr.<sup>3,5</sup>

<sup>1</sup>North Carolina Retina Associates, New Bern, NC, USA;

<sup>2</sup>Bay Area Retina Associates, Walnut Creek, CA, USA;

<sup>3</sup>Neurotech Pharmaceuticals, Cumberland, RI, USA;

<sup>4</sup>Illinois Retina Associates, Joliet, IL, USA; <sup>5</sup>Foundation for Vision Research, Grand Rapids, MI, USA

\*At the time of study conduct

## Purpose

To identify root causes of surgery-related AEs associated with revakinagene taroretcel-Iwey in the treatment of MacTel

## Conclusions

A root cause analysis across six clinical trials of revakinagene taroretcel-Iwey for the treatment of MacTel revealed that surgery-related AEs were primarily driven by surgical technique

Refined surgical protocols and instructions have the potential to significantly reduce AEs and enhance long-term outcomes for individuals with MacTel

## References

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## Disclosures

WLC: Consultant: Amgen, Bayer, Cardinal Health, Genentech/Roche, Neurotech Pharmaceuticals, Ocular Therapeutix, and Regeneron; Grant support: Bayer, EyePoint, Genentech/Roche, Kodiak, Notal Vision, Ocular Therapeutix, Oculus, Outlook, and Regeneron; Speakers bureau: Genentech/Roche and Regeneron; Employee and stock ownership: Annexon Biosciences. RAG: Consultant: Neurotech Pharmaceuticals; Research funding: Lowy Medical Research Institute. JSP: Employment at the time of study conduct: Neurotech Pharmaceuticals; Equity: InnSight Technology, Long Bridge Medical, Notal Vision, PulseMedica, Pykus Therapeutics, Sanulus Medical. TMA: Employee: Foundation for Vision Research and Neurotech Pharmaceuticals; Consulting fees: Castle Biosciences and Regeneron

## Acknowledgments

This analysis was funded by Neurotech Pharmaceuticals.

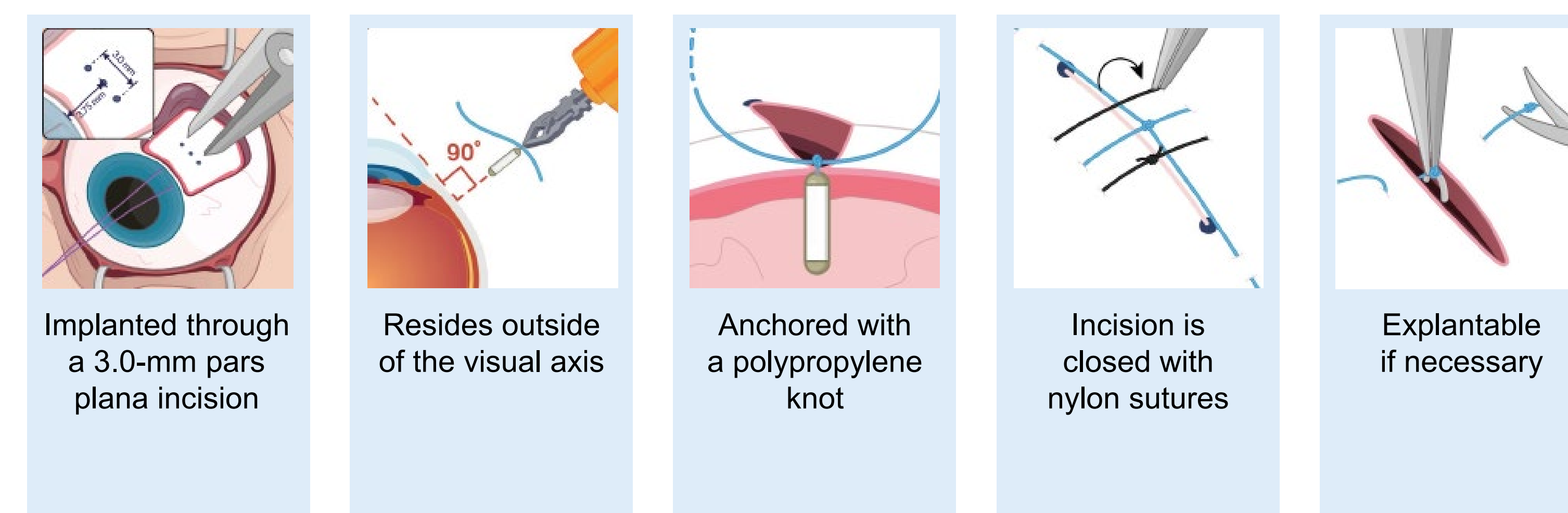
Writing and editorial assistance was provided by Elizabeth McSpirt, MD, MPH, and Christina Mulvihill, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Neurotech.

The investigators would like to thank the Lowy Medical Research Institute and the MacTel Project investigators and their research teams in the Natural History Registry Study and the Phase 1, 2, and 3 clinical trials.

## Background

- Macular telangiectasia type 2 (MacTel) is a bilateral, progressive, retinal neurodegenerative disease that leads to central vision loss and functional impairment<sup>1,2</sup>
- Revakinagene taroretcel-Iwey, approved for the treatment of adults with MacTel, releases bioactive ciliary neurotrophic factor (CNTF) for >14 years following a one-time surgical implantation (Figure 1)<sup>3-5</sup>

Figure 1: Surgical Procedure for Revakinagene Taroretcel-Iwey<sup>3</sup>



## Results

### Surgery-Related Ocular AEs

- Across the six clinical trials, 220 eyes received revakinagene taroretcel-Iwey and 162 eyes underwent sham surgery
- In both groups, investigators considered the majority of ocular AEs to be related to surgery (revakinagene taroretcel-Iwey: **77%**; sham surgery: **68%**)
- Surgery-related AEs occurring in ≥5% of treated eyes are presented in Table 1
  - Of those, four AEs occurred in ≥5% more participants with revakinagene taroretcel-Iwey group than with sham (bolded in Table 1)

Table 1: Surgery-Related Ocular AEs Occurring in ≥5% of Treated Eyes

Surgery-Related Ocular AE, n (%)	Revakinagene Taroretcel-Iwey (n=220)	Sham (n=162)	Difference Between Treatment and Sham (%)
Conjunctival hemorrhage	59 (26.8)	46 (28.4)	-1.6
Eye irritation	52 (23.6)	45 (27.8)	-4.2
<b>Eye pain</b>	<b>46 (20.9)</b>	<b>19 (11.7)</b>	<b>9.2</b>
Vision blurred	45 (20.5)	37 (22.8)	-2.3
Foreign body sensation	25 (11.4)	20 (12.3)	-0.9
<b>Suture-related complication</b>	<b>24 (10.9)</b>	<b>4 (2.5)</b>	<b>8.4</b>
Pruritus	22 (10.0)	11 (6.8)	3.2
<b>Ocular discomfort</b>	<b>21 (9.5)</b>	<b>4 (2.5)</b>	<b>7.0</b>
Conjunctival hyperemia	16 (7.3)	9 (5.6)	1.7
Eye swelling	14 (6.4)	7 (4.3)	2.1
Dry eye	13 (5.9)	6 (3.7)	2.2
<b>Vitreous hemorrhage</b>	<b>13 (5.9)</b>	<b>0</b>	<b>5.9</b>
Conjunctival edema	11 (5.0)	8 (4.9)	0.1
Vitreous floaters	11 (5.0)	1 (0.6)	4.4

AE, adverse event.

- Surgery-related ocular SAEs occurred in 11 (5.0%) eyes with revakinagene taroretcel-Iwey and two (1.2%) eyes with sham surgery (Table 2)

Table 2: Surgery-Related Ocular SAEs

	Revakinagene Taroretcel-Iwey (n=220)	Sham (n=162)
<b>All surgery-related ocular SAEs, n (%)</b>	<b>11 (5.0)</b>	<b>2 (1.2)</b>
Suture-related complication	5 (2.3)	0
Device extrusion	2 (0.9)	0
Vision blurred	2 (0.9)	2 (1.2)
Device expulsion	1 (0.5)	0
Vitreous hemorrhage	1 (0.5)	0

SAE, serious adverse event.

### Vitreous Hemorrhage

- There were 19 cases of vitreous hemorrhage among treated eyes, nine of which were late onset (Figure 3A)
- Analysis showed that cases of late-onset vitreous hemorrhage were due to progressive implant extrusion
  - When an implant begins to extrude, the cap of revakinagene taroretcel-Iwey rubs against the pars plana, creating mechanical chaffing of the uvea and a uveitis-glaucoma-hyphema-like syndrome
  - A case example is shown in Figure 3B; once the conjunctiva was opened, the titanium loop was visible and clearly extruding through the scleral wound (red arrow)

Figure 3: Late-Onset Vitreous Hemorrhage

#### A: Occurrence of Vitreous Hemorrhage

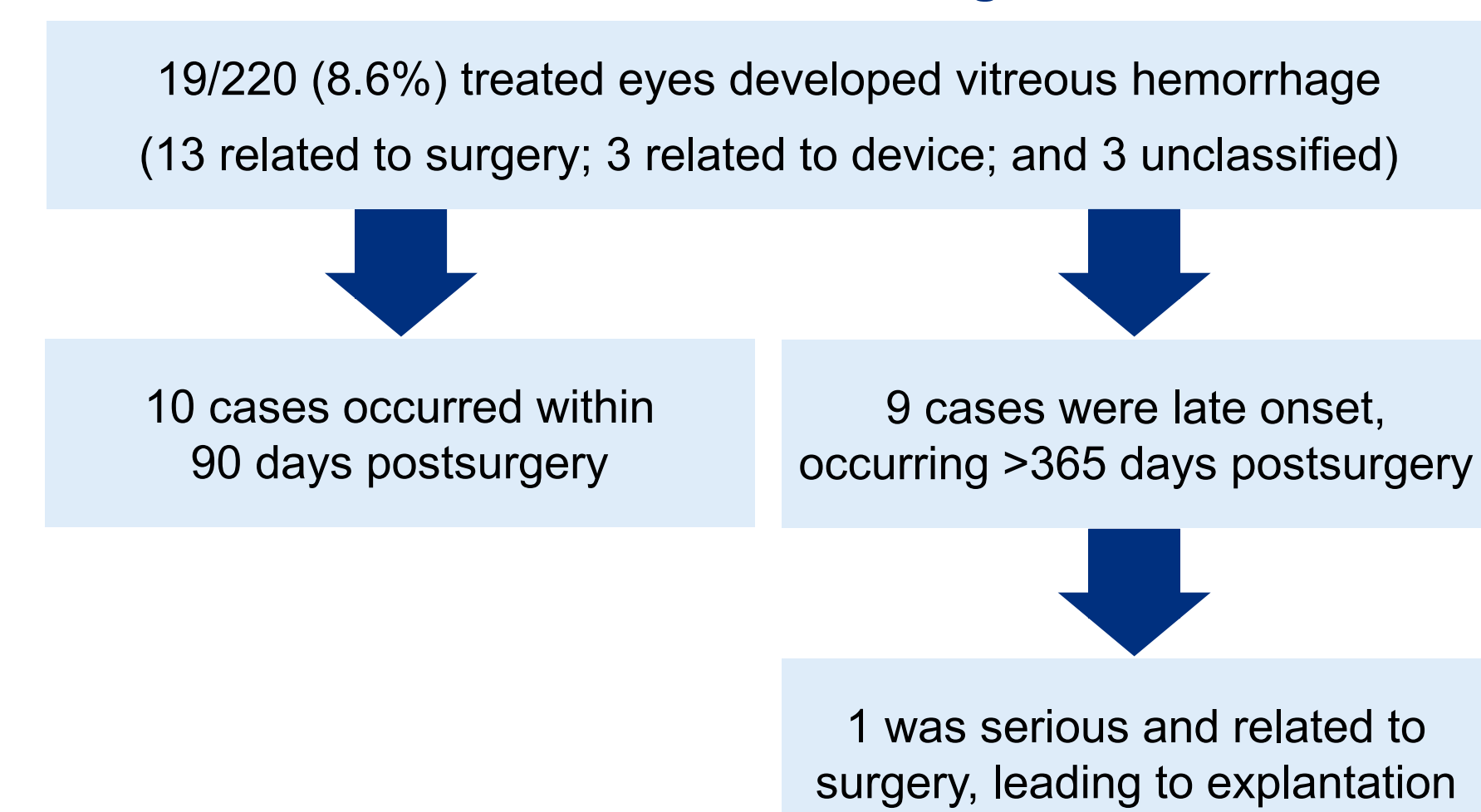


Image provided by Charles C. Wykoff, MD, PhD

#### B: Case of Vitreous Hemorrhage

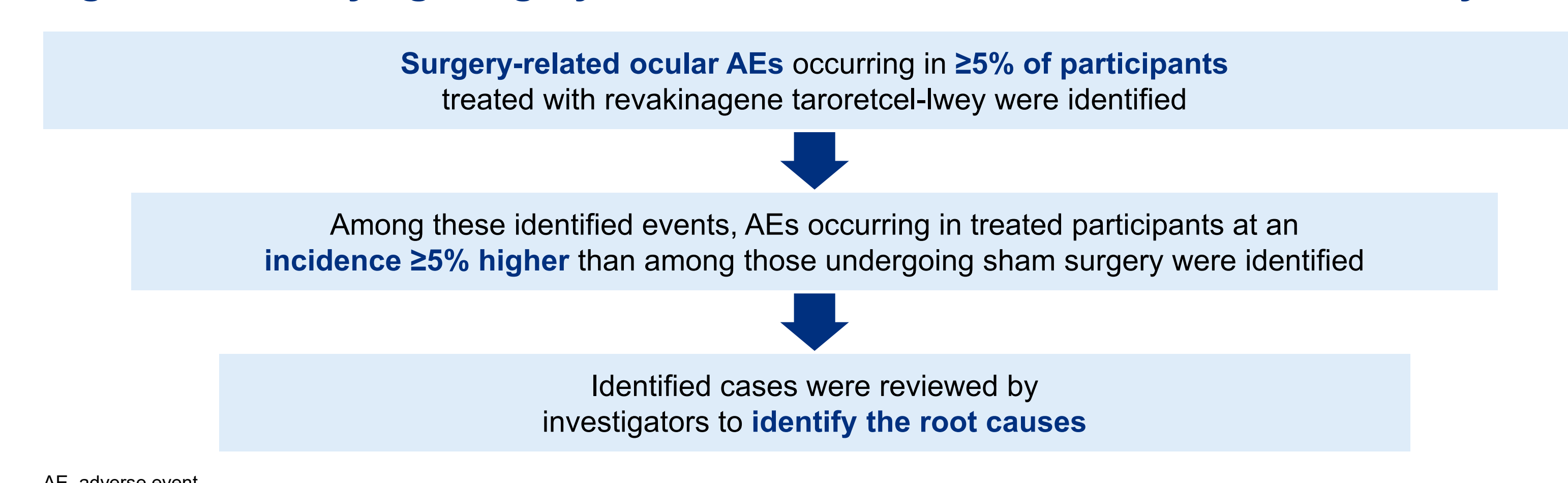


## Methods

- A retrospective examination of ocular adverse events (AEs) and serious AEs (SAEs) from six randomized clinical trials of participants with MacTel was performed<sup>a</sup>
- Data analyzed included an integrated summary of safety, ocular AEs and SAEs, AE reporting forms, surgical reports, and clinic images and surgical videos (if available)
- Certain surgery-related AEs were identified for root cause analysis (Figure 2)

<sup>a</sup>NCT01327911, NCT01949324, NCT04729972, NCT03071965, NCT03316300, NCT03319849.

Figure 2: Identifying Surgery-Related Ocular AEs for the Root Cause Analysis



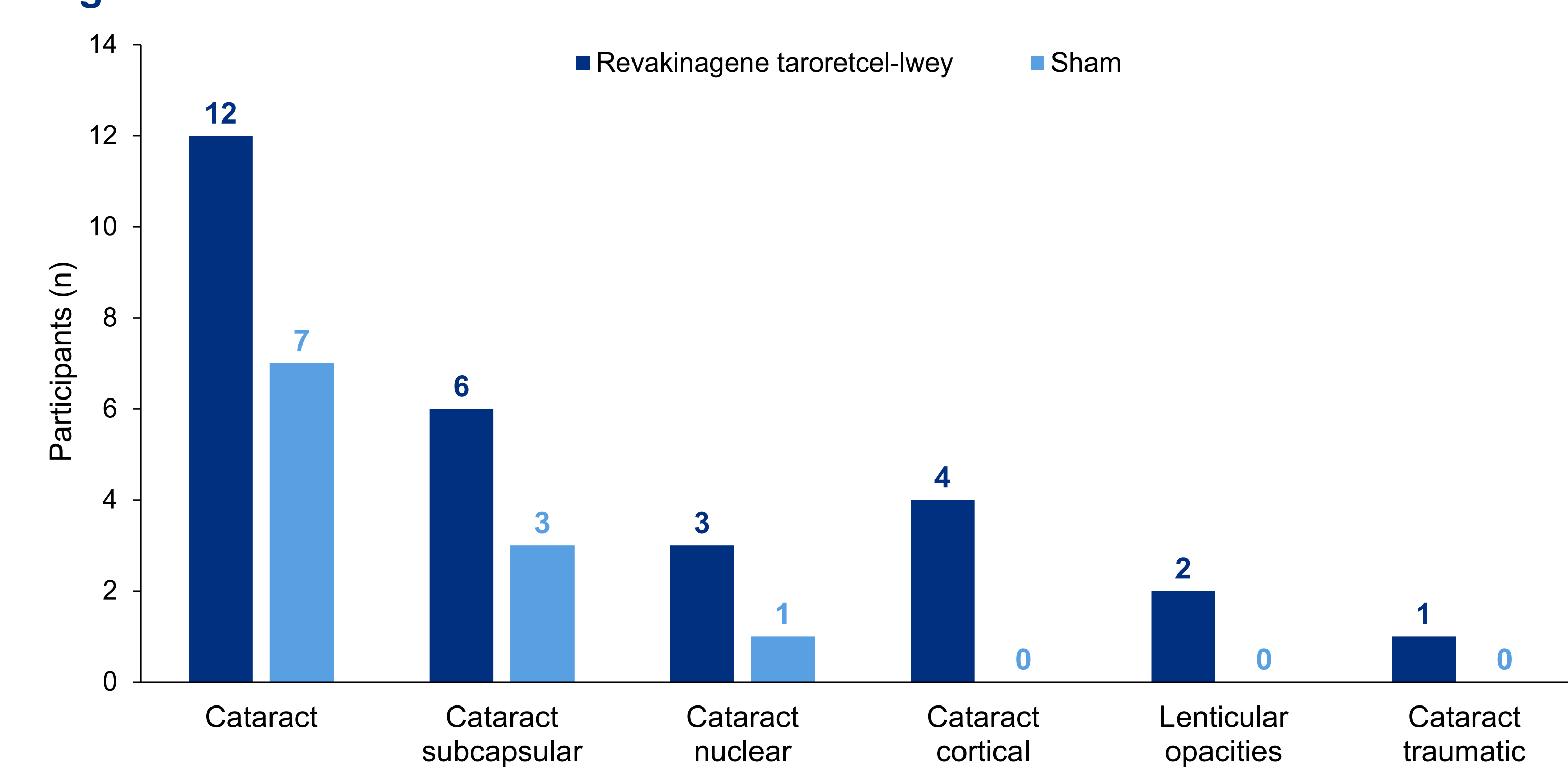
AE, adverse event.

### Cataracts

- All-cause cataract formation (Figure 4) occurred in<sup>a</sup>:
  - 27 treated eyes (12.3%)
  - 11 eyes in the sham group (6.8%)
- The higher rate in treated eyes compared with sham eyes may be due to:
  - Surgical trauma
  - Malpositioned implant
  - CNTF

<sup>a</sup>All-cause cataract was created by combining MedDRA preferred terms of cataract, cataract subcapsular, cataract nuclear, cataract cortical, lenticular opacities, and cataract traumatic.

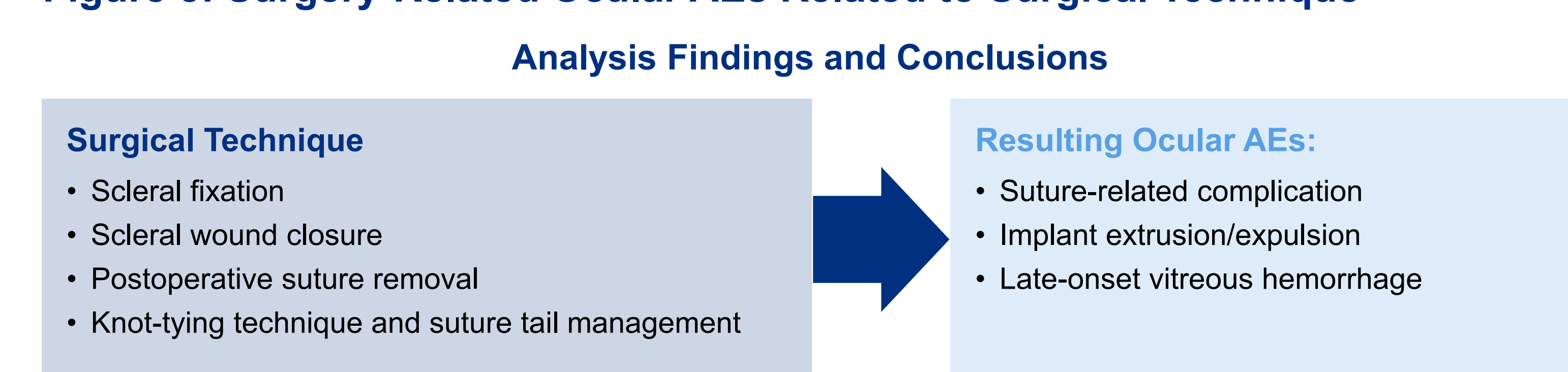
Figure 4: Cataract Formation



### Root Cause: Surgical Technique

- The analysis found that surgical technique resulted in certain surgery-related ocular AEs, such as suture-related complications, device extrusion or expulsion, and late vitreous hemorrhage (Figure 5)

Figure 5: Surgery-Related Ocular AEs Related to Surgical Technique



AE, adverse event.

- Root cause analysis suggests that surgery-related AEs might be mitigated via modified and/or proper:
  - Wound construction
  - Revakinagene taroretcel-Iwey insertion
  - Implant fixation
  - Wound closure
- The findings of this analysis have resulted in surgical procedure changes (Figure 6)

Figure 6: Implementation of Surgical Procedure Changes

