

23RD Euretina
Congress
AMSTERDAM
5-8 October 2023, RAI Amsterdam



Epidemiology, risk factors, pathophysiology and diagnosis of Retinal Vein Occlusion

Irini Chatziralli

Assistant Professor in Ophthalmology

2nd Department of Ophthalmology, University of Athens, Greece

Retinal Vein Occlusion (RVO)

- **Definition:** An obstruction of one of the veins, which drains blood away from the retina
- RVO can lead to severe loss of vision (below driving standards)
- **Classification:** The type of RVO depends on the location of the occlusion

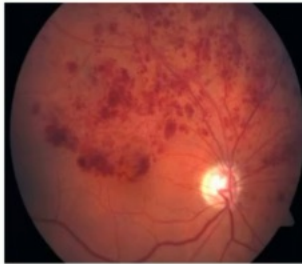
Central Retinal Vein Occlusion (CRVO)

Occlusion of the central retinal vein



Hemiretinal Vein Occlusion (HRVO)

Occlusion of the superior/inferior branch of the central retinal vein
Involves two retinal quadrants



Branch Retinal Vein Occlusion (BRVO)

Occlusion of a branch retinal vein



Percentage of RVO types



20%



80%

Epidemiology

- RVO is the second most common sight-threatening retinal vascular disorder (after diabetic retinopathy)
- Bilaterality: 10% at presentation
- In 1 year, 5% RVO in fellow eye
- The prevalence of RVO increases with age
- The prevalence of RVO did not differ between sexes

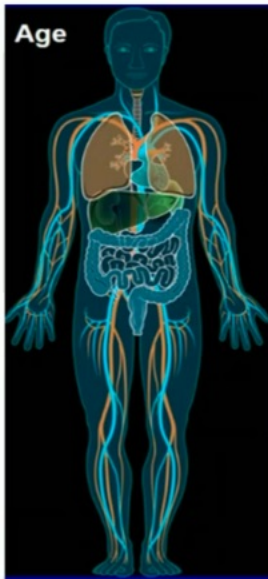
RVO-Risk factors

Ocular diseases

Systemic vascular disorders

Inflammatory/
autoimmune diseases

Various factors



- Glaucoma
- Increased IOP
- Small axial length

- Hypertension
- Diabetes Mellitus
- Hyperlipidemia
- ASCVD

- Systemic Lupus Erythematosus
- Sarcoidosis
- Syphilis
- Takayasu arteritis

- Obesity
- Smoking
- Obstructive sleep apnea
- Renal disease
- Contraception pill use

RVO-Risk factors Young patients

Hematological abnormalities

- Hyperviscosity syndromes
- Coagulation cascade abnormalities
- Protein C, S pathways
- Factor V Leiden
- Factors VII, IX, XI
- Anti-thrombin 3 deficiency
- Myeloproliferative syndromes
- Waldenstrom's macroglobulinemia
- Hyperhomocysteinaemia

- G20210A metlaxix

Mortality, stroke and myocardial infarction

Positive association with RVO

Table 2: Rate of Death, Stroke, Myocardial Infarction after Retinal Vein Occlusion compared to the Cataract Control Cohort

	Death	Stroke	Myocardial infarction	Deep Vein Thrombosis	Pulmonary Embolism
<i>1 year (n= 45303 for each cohort)</i>					
RVO Cohort	2.96%	2.07%	1.31%	1.02%	0.44%
Control Cohort	2.27%	1.28%	1.04%	0.62%	0.46%
Relative Risk (95% CI)	1.30 (1.20, 1.41)	1.61 (1.46, 1.79)	1.26 (1.12, 1.43)	1.65 (1.42, 1.91)	0.98 (0.80, 1.18)
p value	<0.01	<0.01	<0.01	<0.01	0.80
<i>5 year (n= 25024 for each cohort)</i>					
RVO Cohort	23.23%	6.93%	5.52%	2.50%	1.87%
Control Cohort	19.06%	5.22%	4.90%	2.66%	1.97%
Relative Risk (95% CI)	1.22 (1.18, 1.26)	1.33 (1.24, 1.42)	1.13 (1.04, 1.21)	0.94 (0.85, 1.05)	0.95 (0.84, 1.08)
p value	<0.01	<0.01	<0.01	0.94	0.42
<i>10 years (n= 13048 for each cohort)</i>					
RAO Cohort(n=34552)	64.95%	11.02%	9.80%	4.63%	3.40%
Control Cohort (n=34552)	59.93%	9.34%	9.24%	4.40%	3.59%
Relative Risk (95% CI)	1.08 (1.06, 1.10)	1.18 (1.10, 1.27)	1.06 (0.99, 1.14)	1.05 (0.94, 1.18)	0.85 (0.83, 1.08)
p value	<0.01	<0.01	0.12	0.37	0.40

Recommended examinations for all patients

- Blood pressure
- ESR
- Full Blood Count
- Cholesterol, LDL, HDL
- Urea, Creatinine
- Random blood glucose
- Electrolytes
- ECG
- Thyroid function

WHEN SYSTEMIC INVESTIGATION IS MANDATORY

- Lack of usual risk factors
- Present with simultaneous bilateral disease

- Extensive history
- Focus on bleeding/clotting tendency
- Family history with thrombophilia or malignancy

WHEN SYSTEMIC INVESTIGATION IS MANDATORY

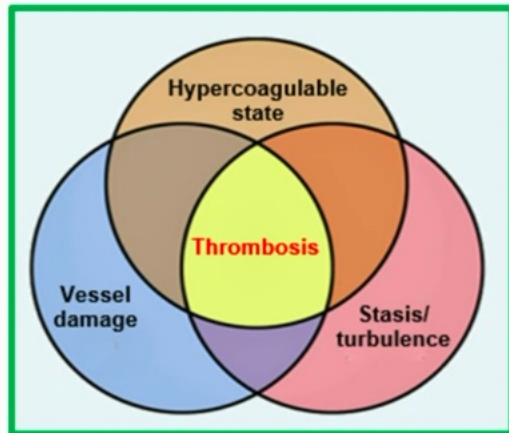
- Lack of usual risk factors
- Present with simultaneous bilateral disease

- Extensive history
- Focus on bleeding/clotting tendency
- Family history with thrombophilia or malignancy

- **The history, ocular examination and initial test results may direct further investigations**

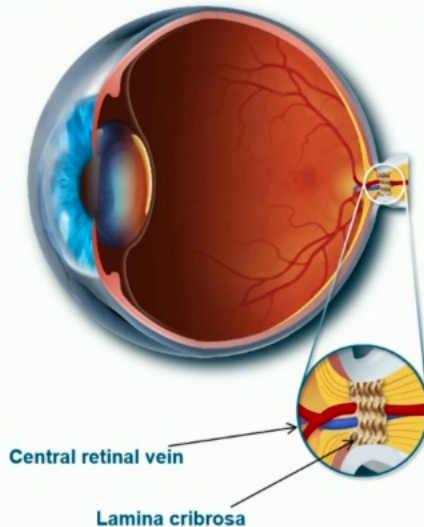
RVO pathogenesis

- Exact pathogenesis of RVO is unclear
- Thrombus formation from changes to Virchow's triad
 - Haemodynamic change resulting in stasis and/or turbulence
 - Vessel wall damage from injury or pathology
 - Hypercoagulability



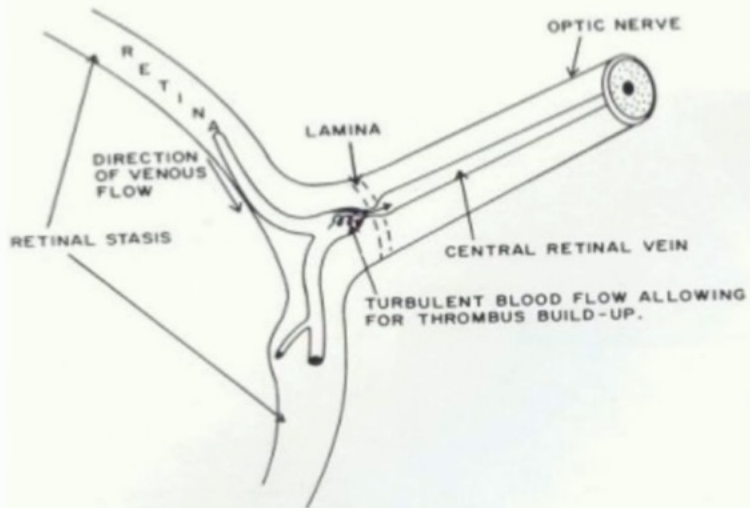
CRVO pathogenesis

CRVO is an occlusion of the central retinal vein in the retrolaminar region of the optic nerve head, due to thrombosis, inflammation or arteriosclerosis



CRVO pathogenesis

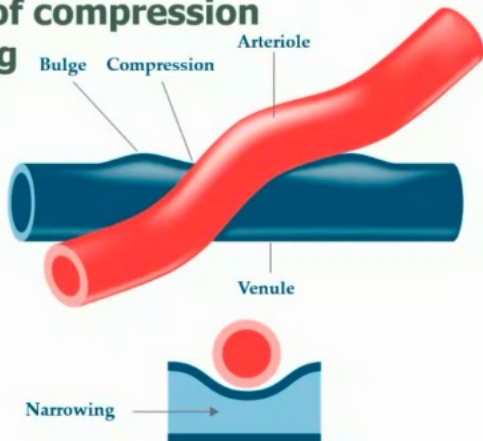
CRVO is an occlusion of the central retinal vein in the retrolaminar region of the optic nerve head, due to thrombosis, inflammation or arteriosclerosis



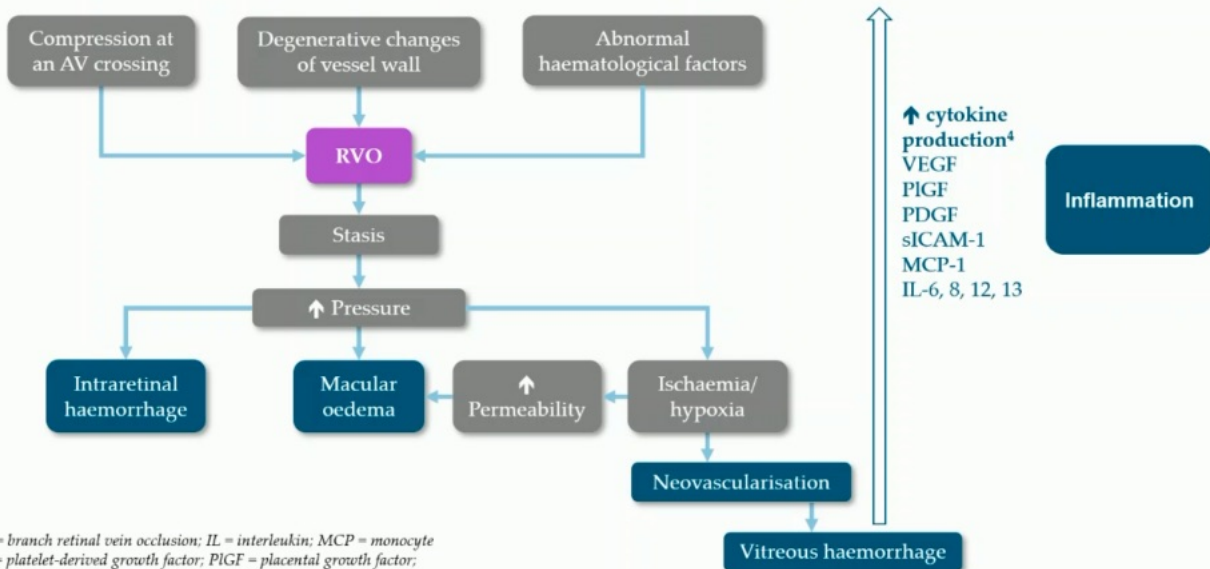
BRVO pathogenesis

BRVO is considered to be the result of compression of a vein at an arteriovenous crossing

- The following features of arteriovenous crossings contribute to the risk of venous occlusion:
 - Artery and vein share a common adventitial sheath¹
 - The artery lies anterior to the affected vein in 99% of eyes with BRVO²
- More than half of BRVO cases occur in the superotemporal quadrant³



RVO pathophysiology



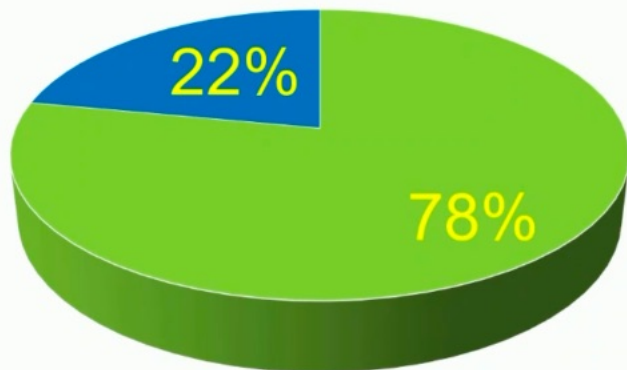
AV = arteriovenous; BRVO = branch retinal vein occlusion; IL = interleukin; MCP = monocyte chemotactic protein; PDGF = platelet-derived growth factor; PIGF = placental growth factor; sICAM-1 = soluble intercellular adhesion molecule; VEGF = vascular endothelial growth factor.

1. Karia N. *Clin Ophthalmol*. 2010;4:809–816; 2. Rehak J, Rehak M. *Curr Eye Res*. 2008;33:111–131; 3. Browning DJ. *Pathophysiology of retinal vein occlusions*. In: *Retinal Vein Occlusions*. New York: Springer Science+Business Media; 2012;

4. Noma H, et al. *Invest Ophthalmol Vis Sci*. 2014;55:3878–3885.

RVO diagnosis



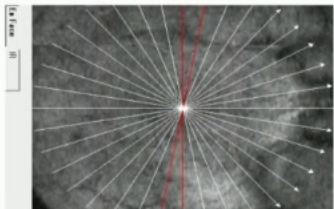
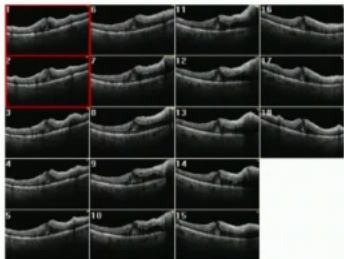


■ Non-ischemic ■ Ischemic

1 in 3 non-ischemic CRVO may progress to ischemic type over 3 years

	Non-ischemic CRVO	Ischemic CRVO
Visual acuity	>20/200	<20/200
RAPD (relative afferent papillary defect)	Mild or absent	present (>0.7 log units of neutral density filter)
Visual field defect	rare	common (use of Goldmann perimeter is suggested, as 30 degree field misses peripheral changes)
Fundus appearance	less disc/macular edema, hemorrhage, cotton-wool spot mild venous tortuosity and dilation	More disc/macular edema, hemorrhage, cotton-wool spot Severe venous tortuosity and dilation
Fundus fluorescein angiogram	less area of nonperfusion	retinal capillary nonperfusion more than 10 disc areas
ERG/electroretinogram	normal	Reduced b wave amplitude ($\leq 60\%$ of the normal mean value of both photopic and scotopic ERG), and reduced b/a
Prognosis	good, less chance of anterior segment neovascularization/neovascular glaucoma	Poor, high chance of anterior segment neovascularization/neovascular glaucoma The visual prognosis may be worse than central retinal arterial occlusion

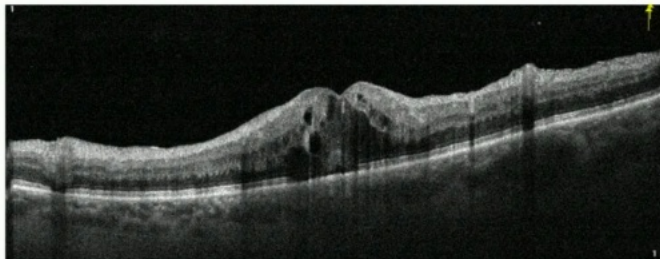
Radial Lines



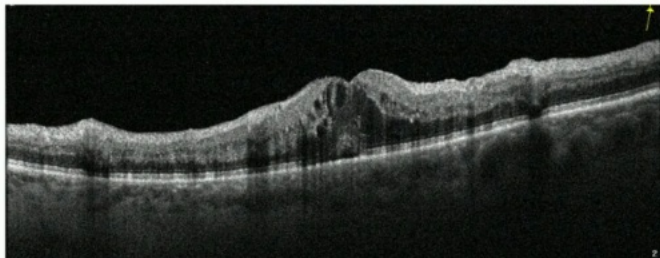
Print

Signal Strength Index 49

Right / OD



1x1 3x2 2x2 Auto Zoom 10.00 Scan Size (mm)

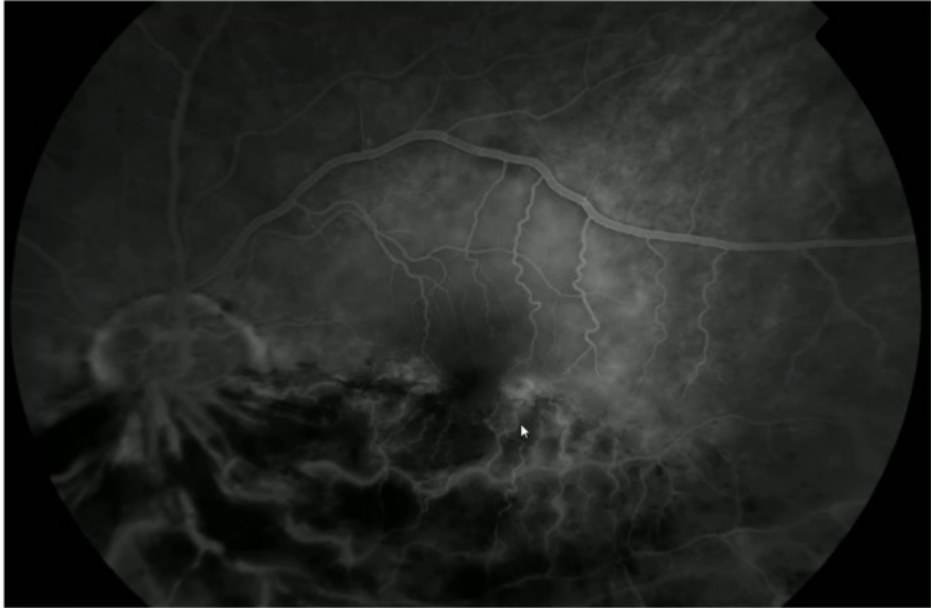


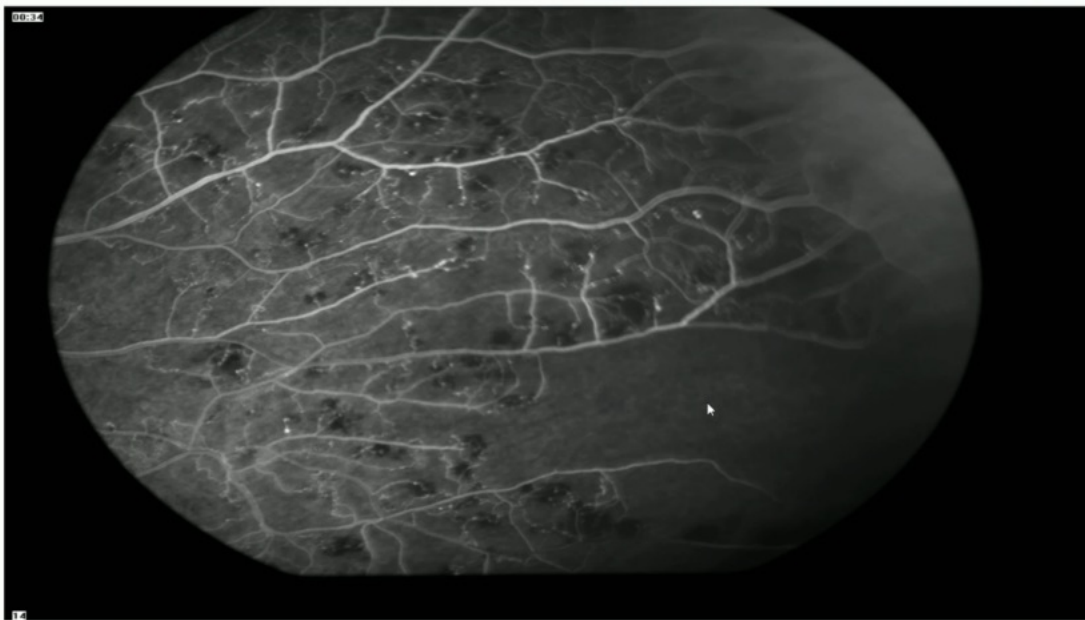
Comment



Fluorescein angiography (FFA)

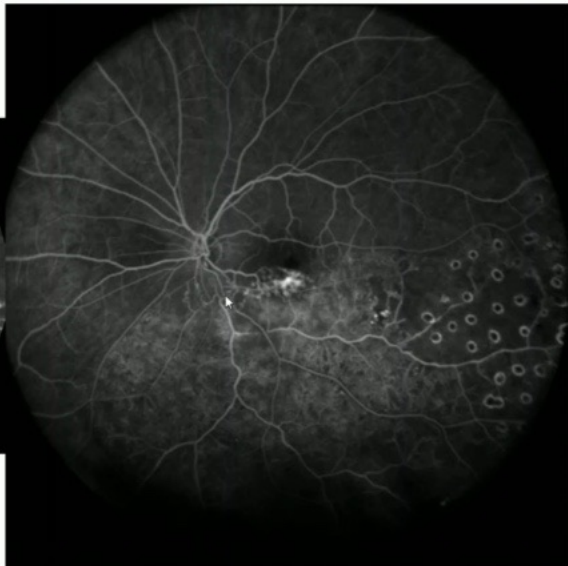




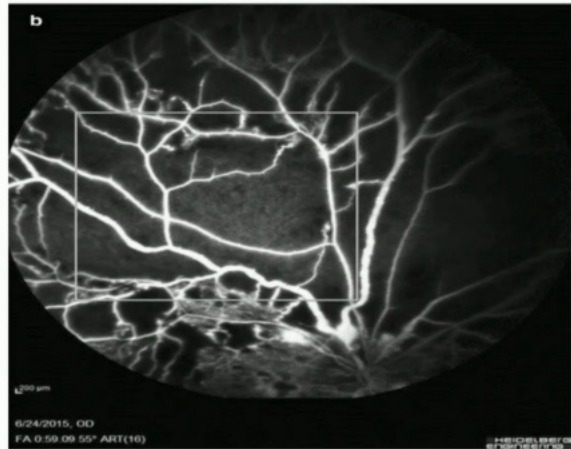
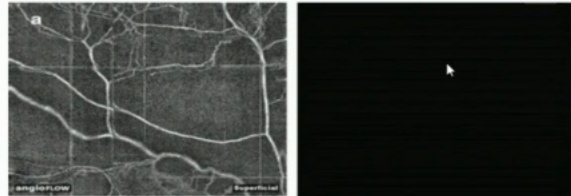
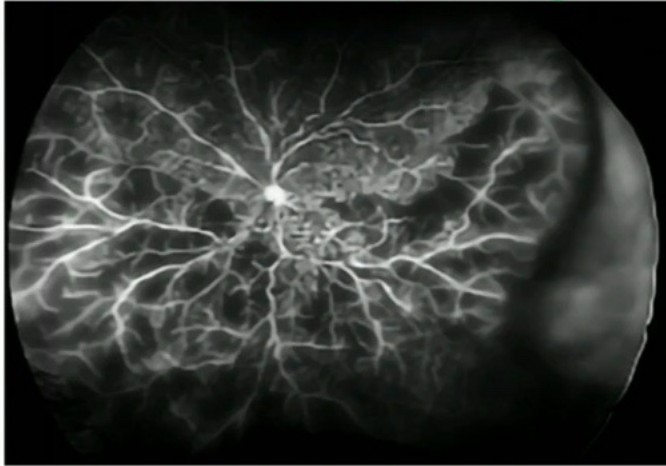




Ultrawidefield FFA



FFA - periphery



OCT-Angiography (OCT-A)

Angio Retina

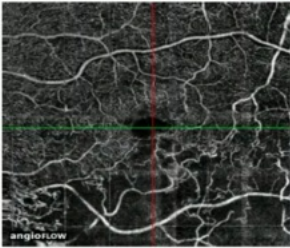
Signal Strength Index 62

Left / OS

6.00 x 6.00 Scan Size (mm)

Save Ango

Measure
OR



3D Display

OverView

Play

Show Brd
 No MCT
 Color
 Show Line

Save Settings

Restore Settings

Reference
 Superficial
 Deep
 Outer Retina
 Chorioid Gap

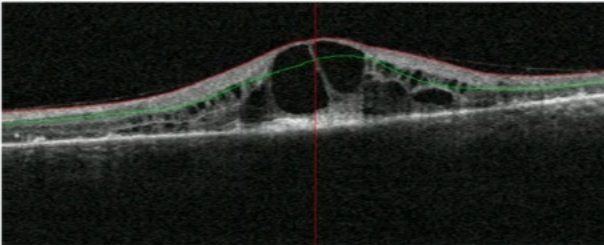
Upper - 3.4
Offset(Lin)

3 mm

Lower - 3.1
Offset(Lin)

14 mm


FLatten Brd



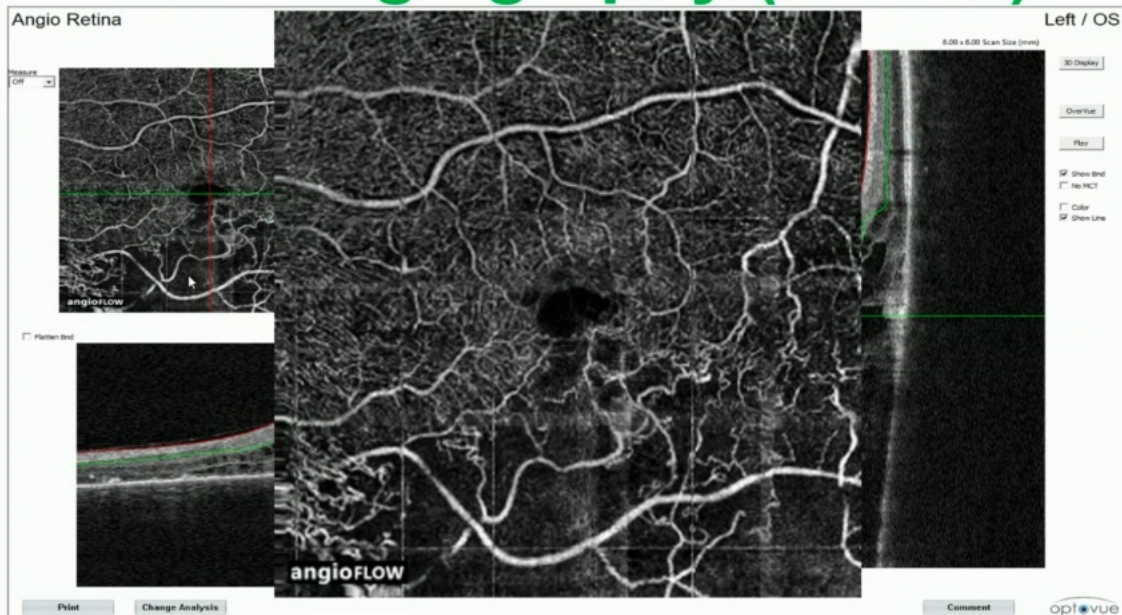
Print

Change Analysis

Comment



OCT-Angiography (OCT-A)



Conclusions

- RVO is the 2nd most common sight-threatening retinal vascular disorder
- Several **risk factors** have been identified, with hypertension to be the most significant
- Important to check for risk factors and manage them
- Do selectively extensive work-up
- The history, ocular examination and initial test results may direct further investigations
- **Pathophysiologically**, the main pathways involve inflammation and increase of VEGF
- **Macular edema and ischemia** are the most common causes of visual loss
- **OCT** is the main imaging modality to confirm and follow-up macular edema, while **FFA** is useful to evaluate non-perfusion

23RD Euretina
Congress
AMSTERDAM

5-8 October 2023, RAI Amsterdam



I.R.C.C.S. Ospedale
San Raffaele

Gruppo San Donato



Retinal Vein Occlusion: From Pathophysiology To Treatment

Imaging biomarkers and anti-VEGF for macular edema due to RVO

Maria Vittoria Cicinelli

Università Vita-Salute San Raffaele

Milano

Chairman: Prof. Francesco Bandello

Issues dealing with RVO:

Heterogeneity in baseline VA, treatment response, # of injections

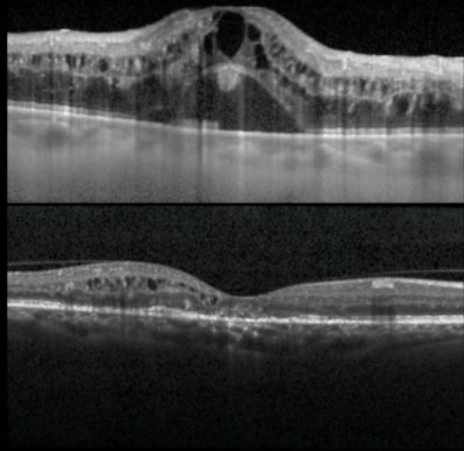
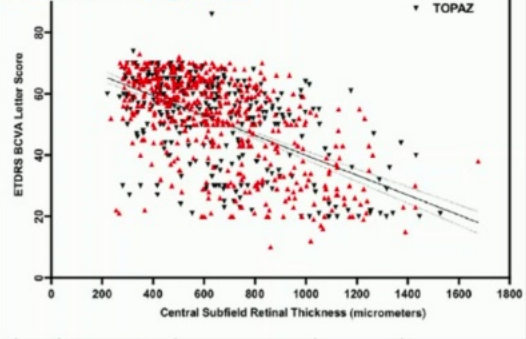


Modest correlation between VA and macular thickness

Randomized Controlled Trial | Ophthalmol Retina. 2021 Jul;5(7):633-647.
doi: 10.1016/j.oret.2020.10.016. Epub 2020 Oct 29.

Visual Acuity in Retinal Vein Occlusion, Diabetic, and Uveitic Macular Edema: Central Subfield Thickness and Ellipsoid Zone Analysis

Thomas A Ciulla¹, Barry Kapik², Dbraj S Ghosal³, Michael S Ip⁴
Affiliations + expand
PMID: 33130256 DOI: 10.1016/j.oret.2020.10.016



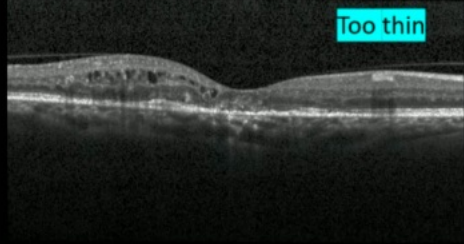
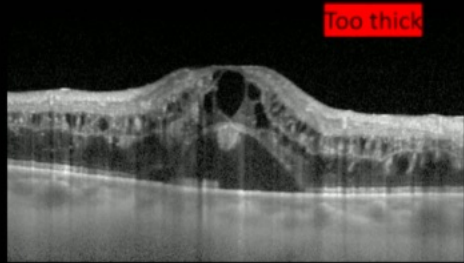
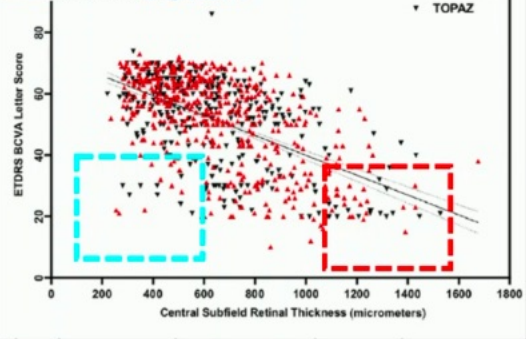
Issues dealing with RVO:

Modest correlation between VA and macular thickness

Randomized Controlled Trial | Ophthalmol Retina. 2021 Jul;5(7):633-642.
doi: 10.1016/j.oret.2020.10.016. Epub 2020 Oct 29.

Visual Acuity in Retinal Vein Occlusion, Diabetic, and Uveitic Macular Edema: Central Subfield Thickness and Ellipsoid Zone Analysis

Thomas A Ciulla¹, Barry Kapik², Dbraj S Grewal³, Michael S Ip⁴
Affiliations + expand
PMID: 33130256 DOI: 10.1016/j.oret.2020.10.016



Low presenting VA
Poor VA outcomes

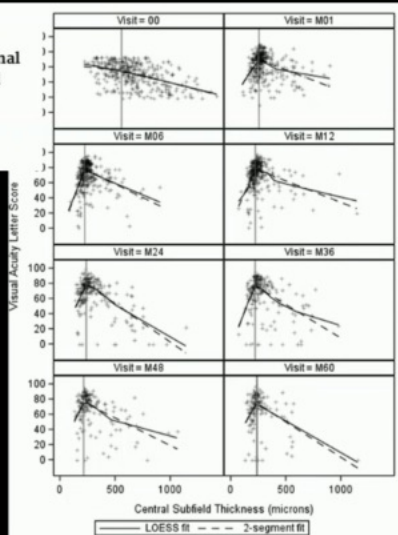
NON-LINEAR FIT

> Ophthalmology. 2023 Oct;130(10):1066-1072. doi: 10.1016/j.ophtha.2023.05.023. Epub 2023 May 21.

SCORE2 Report 24: Nonlinear Relationship of Retinal Thickness and Visual Acuity in Central Retinal and Hemiretinal Vein Occlusion

Ingrid U Scott ¹, Neal L Oden ², Paul C VanVeldhuisen ³, Michael S Ip ⁴, Barbara A Blodi ⁵; SCORE2 Investigator Group

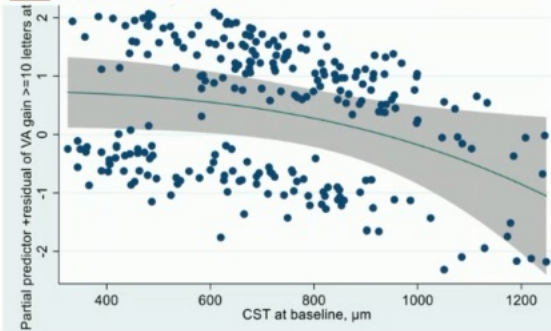
Affiliations + expand



Randomized Controlled Trial > Ophthalmol Retina. 2021 Nov;5(11):1115-1124. doi: 10.1016/j.oret.2021.02.008. Epub 2021 Feb 19.

Predictors of Visual Acuity Outcomes after Anti-Vascular Endothelial Growth Factor Treatment for Macular Edema Secondary to Central Retinal Vein Occlusion

Piyali Sen ¹, Sarega Gurudas ², Jayashree Ramu ³, Namritha Patrao ³, Shrutli Chandra ¹, Rajna Rasheed ³, Luke Nicholson ³, Tunde Peto ⁴, Sobha Sivaprasad ⁵, Philip Hykin ¹



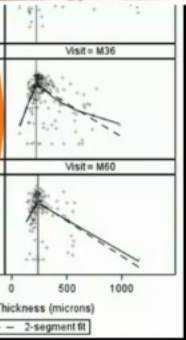


> Ophthalmology. 2023 Oct;130(10):1066-1072. doi: 10.1016/j.ophtha.2023.05.023. Epub 2023 May 21.

SCORE2 Report 24: Nonlinear Relationship of Retinal Thickness and Visual Acuity in Central Retinal and Hemiretinal Vein Occlusion

Ingrid U Scott ¹, Neal L Oden ², Paul C VanVeldhuisen ³, Michael S In ⁴, Barbara A Blodi ⁵; SCORE2 Investigator Group

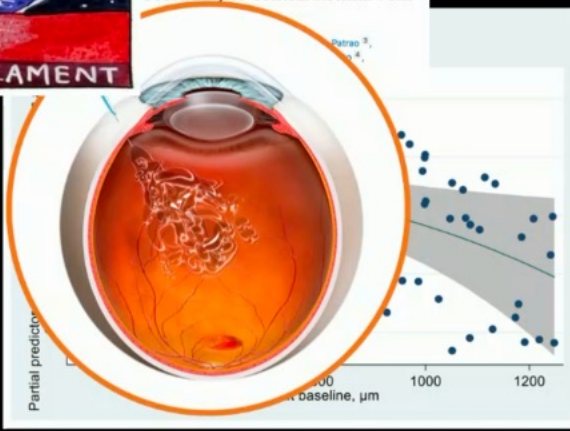
Affiliations: + expand



> Ophthalmol Retina. 2021 Nov;5(11):1115-1124. Epub 2021 Feb 19.

Visual Acuity Outcomes after Anti-vascular Endothelial Growth Factor Treatment for Secondary to Central Retinal Vein Occlusion

Patrao ¹, ...



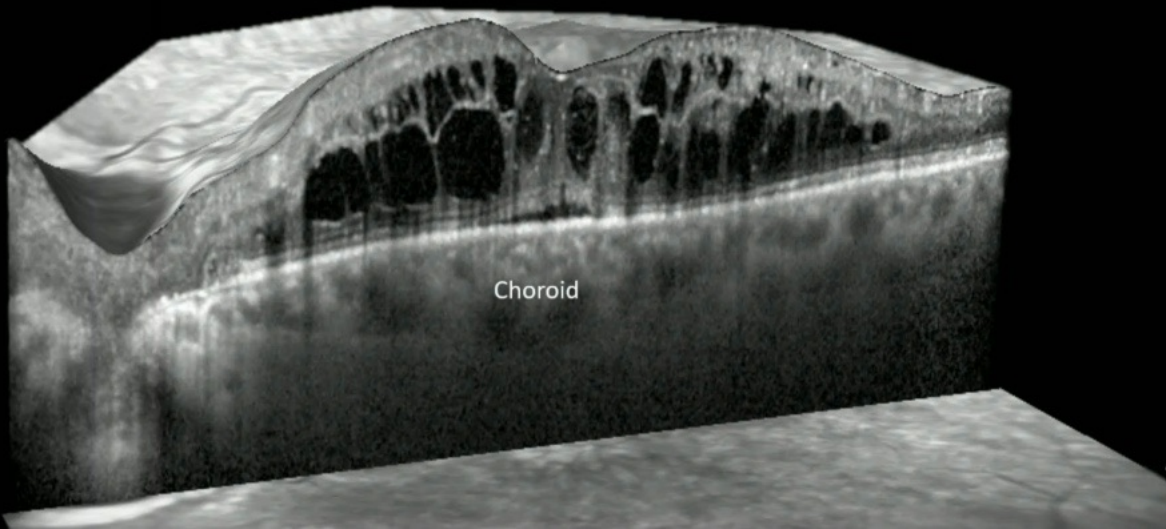
The impact of structural optical coherence tomography changes on visual function in retinal vein occlusion



Martin Michl¹, Xuhui Liu^{1, 2}, Alexandra Kaider³, Amir Sedeghipour¹,
Blanca S Gerendas¹, Ursula Schmidt-Ertursh¹

Affiliations + expand

Vitreoretinal interface

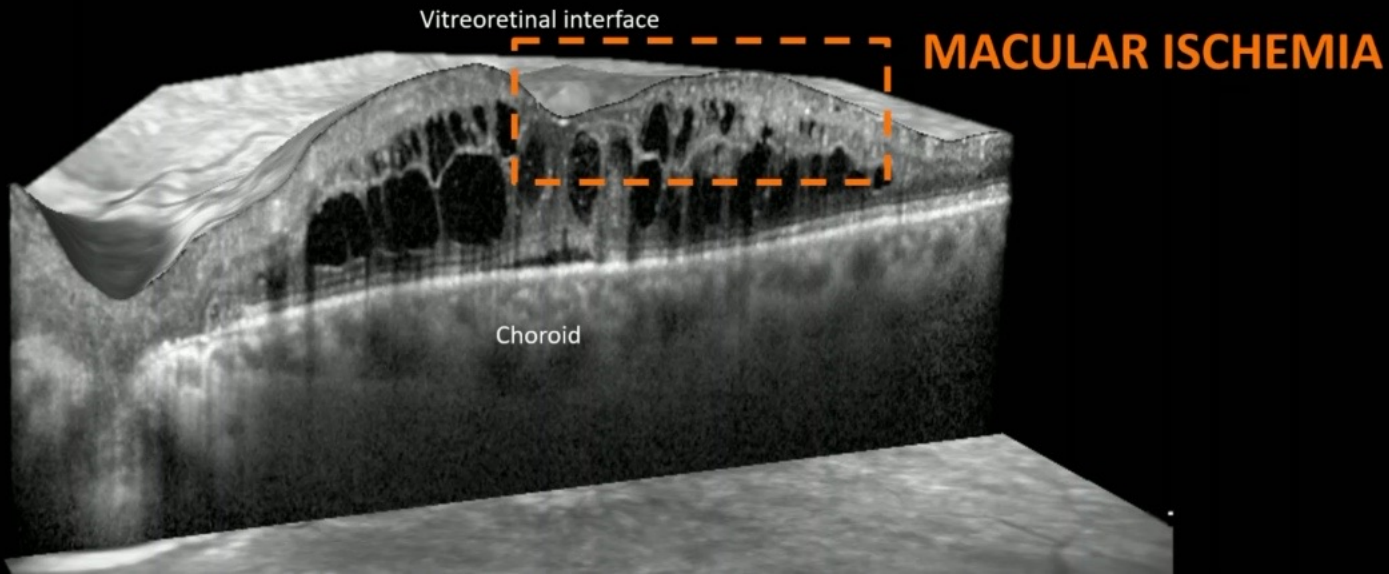


The impact of structural optical coherence tomography changes on visual function in retinal vein occlusion



Martin Michl¹, Xuhui Liu^{1,2}, Alexandra Kaider³, Amir Sadeghipour¹,
Blanca S Gerendas¹, Ursula Schmidt-Erfurth¹

Affiliations + expand

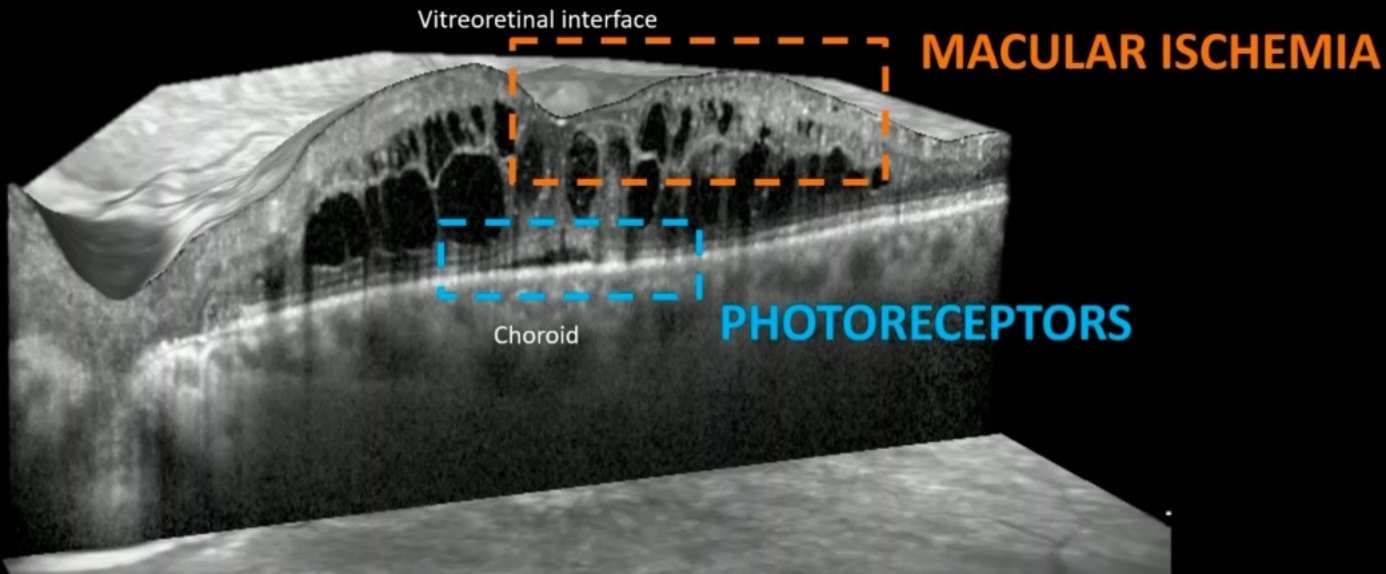


The impact of structural optical coherence tomography changes on visual function in retinal vein occlusion



Martin Michl¹, Xuhui Liu^{1,2}, Alexandra Kaider³, Amir Sadeghipour¹,
Blanca S Gerendas¹, Ursula Schmidt-Ertursh¹

Affiliations + expand

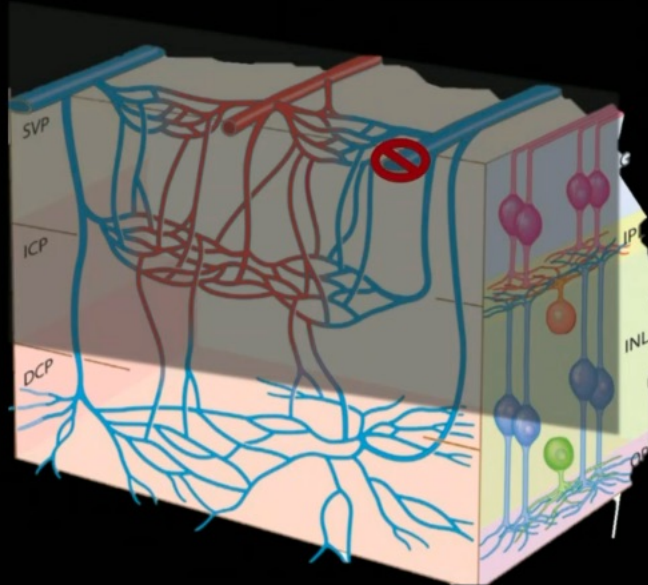


MACULAR ISCHEMIA

OCT Grading System of Macular Infarction Predicts Vision in Participants With Central Retinal or Hemiretinal Vein Occlusion: A Secondary Analysis of SCORE2

Adrian Au¹, Michael Ip², Barbara A Stoll³, Ingrid U Scott⁴, Neal L Oden⁵, Paul C Van Velthuisen⁶, David Sarraf⁷

IRB Affiliations + expand



Hydrostatic pressure in DCP venules

MACULAR ISCHEMIA

OCT Grading System of Macular Infarction Predicts Vision in Participants With Central Retinal or Hemiretinal Vein Occlusion: A Secondary Analysis of SCORE2

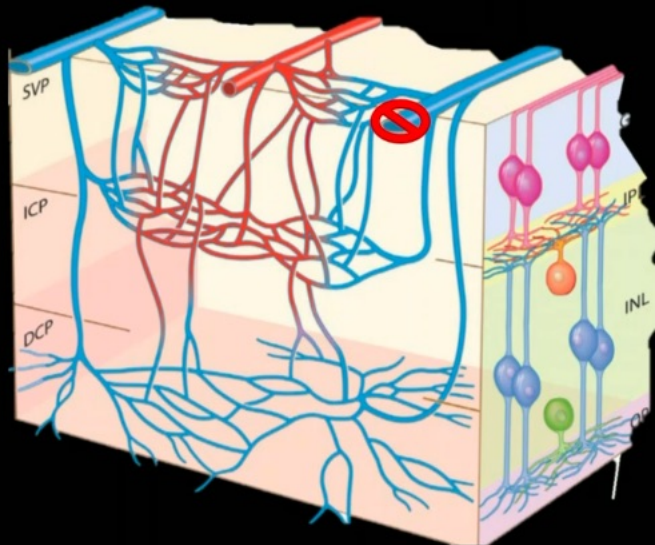
Adrian Au¹, Michael Ip², Barbara A Stob³, Ingrid U Scott⁴, Neal L Oden⁵, Paul C Van Velthuisen⁶, David Sarraf⁶

MRB

Affiliations + expand

↓ Perfusion pressure from SVP arterioles

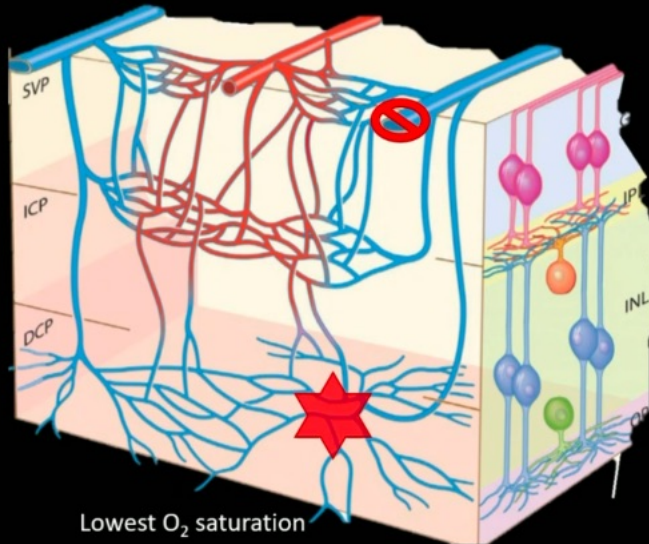
↑ Hydrostatic pressure in DCP venules



MACULAR ISCHEMIA

Perfusion pressure from SVP arterioles

Hydrostatic pressure in DCP venules



OCT Grading System of Macular Infarction Predicts Vision in Participants With Central Retinal or Hemiretinal Vein Occlusion: A Secondary Analysis of SCORE2

Adrian Au¹, Michael Ip², Barbara A Stob³, Ingrid U Scott⁴, Neal L Oden⁵, Paul C Van Velthuisen⁶, David Sarraf⁶

MRB Affiliations + expand

MACULAR ISCHEMIA

OCT Grading System of Macular Infarction Predicts Vision in Participants With Central Retinal or Hemiretinal Vein Occlusion: A Secondary Analysis of SCORE2

Adrian Au¹, Michael Ip², Barbara A Stob³, Ingrid U Scott⁴, Neal L Oden⁵, Paul C Van Veldhuisen⁶, David Sarraf⁶

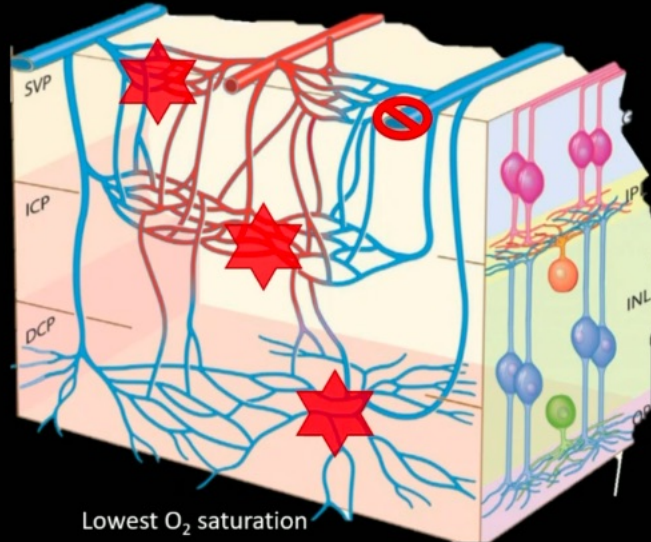
MRB Affiliations + expand



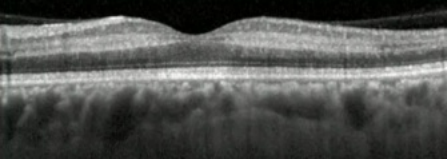
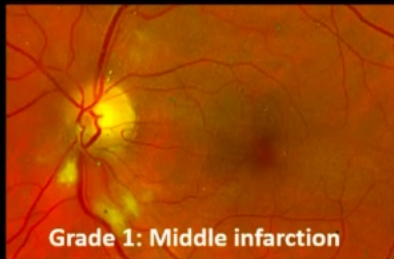
Perfusion pressure from SVP arterioles



Hydrostatic pressure in DCP venules

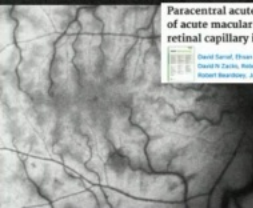


THE ISCHEMIC CASCADE

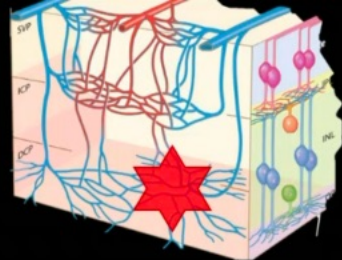


Paracentral acute middle maculopathy: a new variant of acute macular neuroretinopathy associated with retinal capillary ischemia

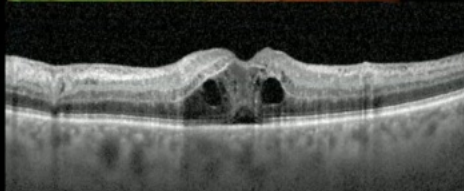
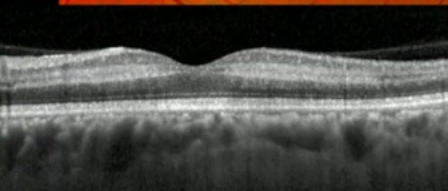
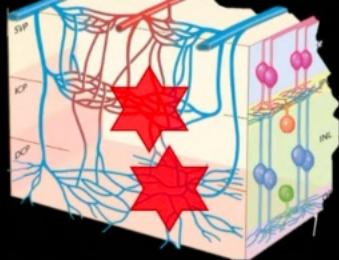
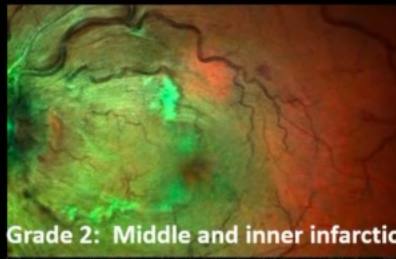
David Sarraf, Ethan Rahimy, Anwar A. Fawc, Elhad Sofin, Ewan Barakatt,
David H. Zachs, Robert A. Mills, James W. Kyrleuk, Jr., Sarah Mages, Neema P. Goshberg,
Robert Burchette, John A. Sorenson, & Stanley Prasad



PAMM



THE ISCHEMIC CASCADE

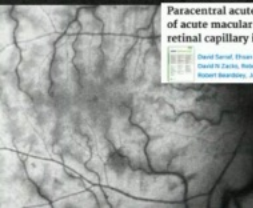


Paracentral acute middle maculopathy: a new variant of acute macular neuroretinopathy associated with retinal capillary ischemia

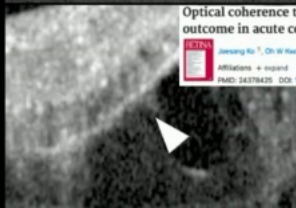
David Sarraf, Ehsan Rahimi, Anand A. Patel, Elhad Salah, Farah Barakat, David H. Zacks, Robert A. Miller, James M. Karavonis, Sarah Mages, Nasser H. Ghalibeg, Robert Swartzberg, John A. Sorenson, & Stanley Prasad

Optical coherence tomography predicts visual outcome in acute central retinal vein occlusion

Jeejung Ko¹, Ch W Heon, Suk H Byeon
Affiliations + expand
PMID: 24378425 DOI: 10.1097/AE.0000000000000054

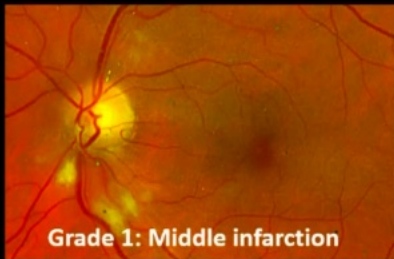
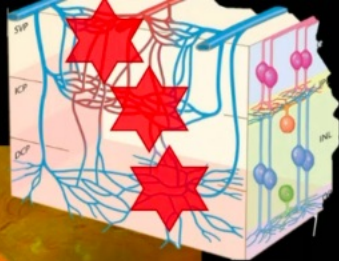


PAMM

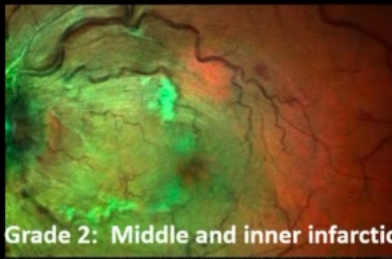


p-MLM

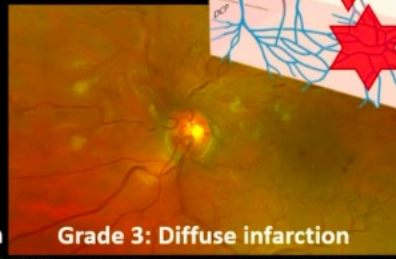
THE ISCHEMIC CASCADE



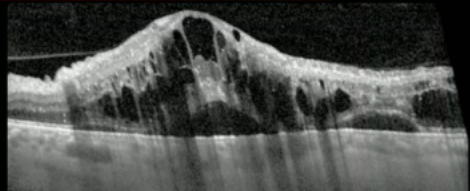
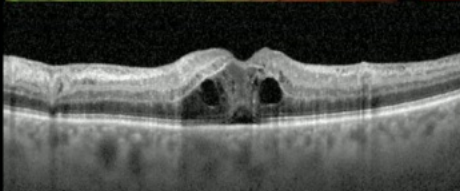
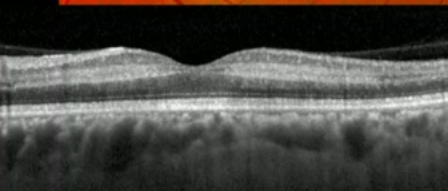
Grade 1: Middle infarction



Grade 2: Middle and inner infarction



Grade 3: Diffuse infarction



Paracentral acute middle maculopathy: a new variant of acute macular neuroretinopathy associated with retinal capillary ischemia

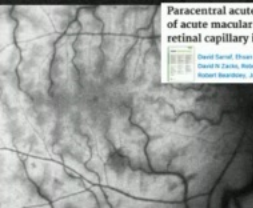
David Sarraf, Shuan Rahimy, Anupriya Fawcett, Elliot Sohn, Irene Barakowitz, David H Zacks, Robert A Miller, James W Kiaravick, Jr., Sarah Argen, Navin R Giddeberg, Robert Swartzberg, John A Sorenson, & Stanley Freund

Optical coherence tomography predicts visual outcome in acute central retinal vein occlusion

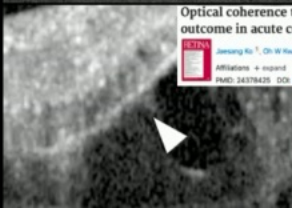
Jeejung Ko¹, Oh W Kwon, Suk H Byeon
Affiliations + expand
PMID: 24379425 DOI: 10.1007/sae.0000000000000064

Increased Inner Retinal Layer Reflectivity in Eyes With Acute CRVO Correlates With Worse Visual Outcomes at 12 Months

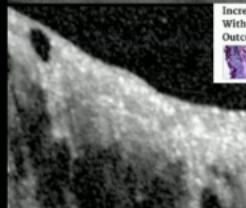
Wilson Marini¹, Fabio Lanzetta², Sara Gallozza³, Michael Suter⁴, Kenneth J Hodge⁵, Michael Williams⁶, Gadi Weizman⁷, Carl Schuman⁸, & Stanley Freund¹, Study Group⁹, Stephen Wong¹⁰



PAMM

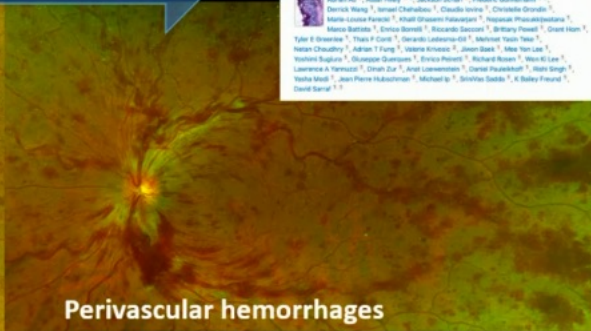
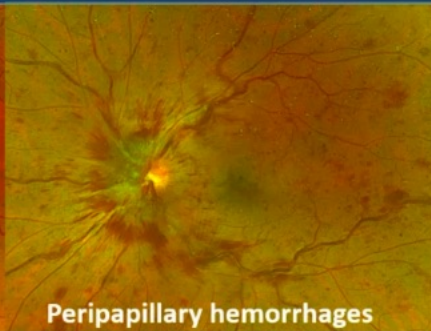
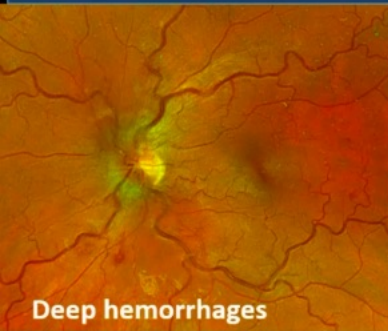


p-MLM



HYPER REFLECTIVITY

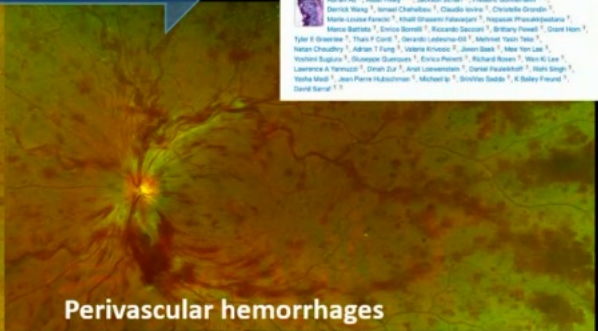
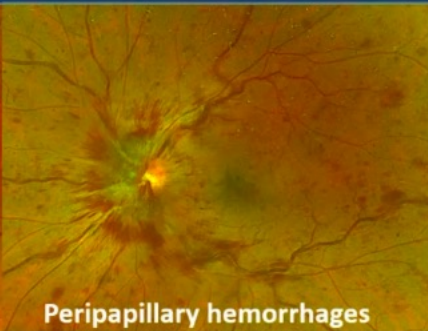
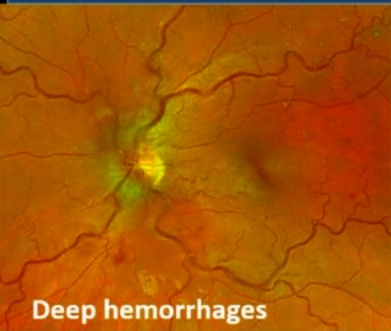
THE ISCHEMIC CASCADE



Relationship Between Nerve Fiber Layer Hemorrhages and Outcomes in Central Retinal Vein Occlusion

Adrian Au¹, Assad Hsieh¹, Jackson Schiff¹, Frederic Ganssmann¹,
Derrick Wang¹, Samuel Chhabra¹, Claudia Ivorra¹, Christine Grondin¹,
Marie-Louise Paré¹, Khalil Ghassam Fawcett¹, Rajwanth Phasakulwattana¹,
Marco Battista¹, Evine Demirel¹, Riccardo Sacconi¹, Bikram Poudel¹, David Han¹,
Tyler E Dwanke¹, Thilo P Durr¹, Saraaki Lubiana-Gil¹, Michael Tsai¹,
Nehal Choudhry¹, Adrian T Fung¹, Sabine Krusele¹, Joon Baik¹, Mia-Yon Lee¹,
Yoshimi Suguro¹, Giuseppe Quaresima¹, Enrico Piretti¹, Richard Rosen¹, Wen Ki Lee¹,
Lawrence A Hernandez¹, Dinah Zur¹, Amit Laxwani¹, Daniel Hausknecht¹, Haro Singh¹,
Yusuf Saifi¹, Jean Pierre Hubichman¹, Michael Ip¹, Sorintra Saitta¹, et Bailey Freund¹,
David Sarda¹

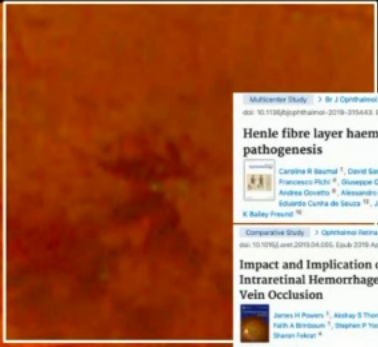
THE ISCHEMIC CASCADE



Observational Study | *J Inher Metab Dis* 2020; 43(10):2133-44
doi: 10.1007/s10848-020-01334-4

Relationship Between Nerve Fiber Layer Hemorrhages and Outcomes in Central Retinal Vein Occlusion

Adrian Au¹, Asad Hsieh^{1,2}, Jackson Schott¹, Frederic Guimaraes^{1,3}, Derrick Wang¹, Sameer Chhablani¹, Claudio Savino¹, Christine Grondin¹, Marie-Louise Fawcett¹, Khalil Ghazem Faragani¹, Rossini Prasad Kowlansa¹, Marco Barileto¹, Enrico Bombi¹, Riccardo Sacconi¹, Brijesh Purohit¹, David Han¹, Tyler E Shewler¹, Thais F Dard¹, Saraali Lohman-Gil¹, Mehmet Yasin Taka¹, Nathan Choudhry¹, Adrian T Fung¹, Vidula Krishna¹, Jovan Baek¹, Mei-Yen Lee¹, Vincent Suglione¹, Giuseppe Guimaraes¹, Erica Peiretti¹, Richard Rosen¹, Wen-Ki Lee¹, Lawrence A Hernandez¹, Dhan Zur¹, Amit Laxwanshi¹, Daniel Hausknecht¹, Harsh Singh¹, Yehia Said¹, Jean Pierre Hublotshman¹, Michael Ip¹, Srinivas Sooda¹, K Bailey Freund¹, David Sarraf^{1,2}



Multicenter Study | *J Clin Ophthalmol*. 2021 Mar;105(3):374-380.
doi: 10.1097/Ophth.0000000000002054. Epub 2020 May 6.

Henle fibre layer haemorrhage: clinical features and pathogenesis

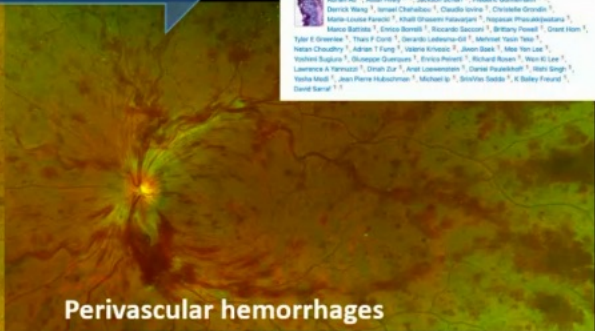
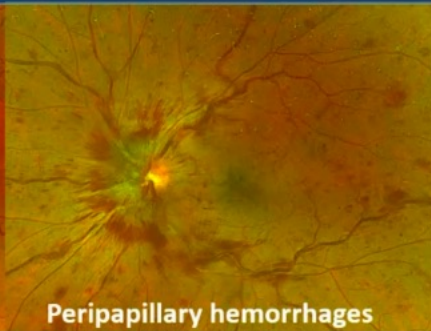
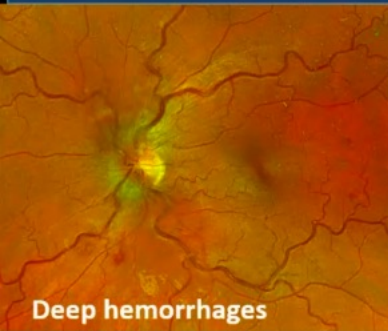
Caroline R Baumal¹, David Sarraf¹, Tara Bryant¹, Wei Gu¹, Nora Mukhtasov¹, Francesco Pichi¹, Giuseppe Quaresima¹, Nathan Choudhry¹, Mehmet Yasin Taka¹, Andrea Govetto¹, Alessandro Invernizzi¹, Dean Elliott¹, Adin Gaudin¹, Eduardo Cunha de Saiva¹, Jonathan Nussan¹, Andrea Lembo¹, Grace C Lee¹, K Bailey Freund¹

Comparative Study | *J Ophthalmol Retina*. 2019 Sep;9(9):790-796.
doi: 10.1097/OPT.0000000000000505. Epub 2019 Apr 10.

Impact and Implication of Fovea-Involving Intraretinal Hemorrhage after Acute Branch Retinal Vein Occlusion

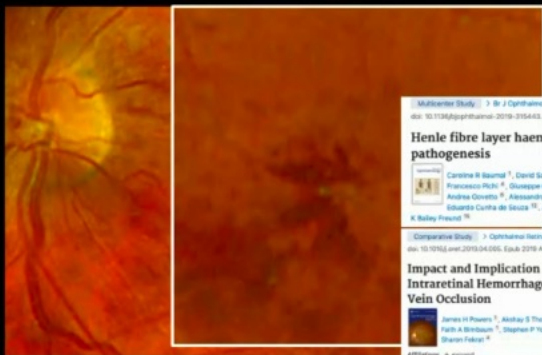
James H Powers¹, Akshay S Thomas¹, Tahseen A Mir¹, Jane S Kim¹, Faith A Binneman¹, Stephen P Yoon¹, Kira Khan¹, Maria Gomez-Caraballo¹, Sharon Felker¹

THE ISCHEMIC CASCADE



Relationship Between Nerve Fiber Layer Hemorrhages and Outcomes in Central Retinal Vein Occlusion

Adnan Au¹, Asad Hsieh¹, Jackson Schott¹, Frederic Guimaraes¹, Derrick Wang¹, Sameer Chhabab¹, Claudio Iovine¹, Christophe Grandjean¹, Marie-Louise Pascale¹, Khalil Ghazem Faragani¹, Nageswari Prasadakrishnan¹, Marco Battista¹, Cinzia Bernini¹, Riccardo Sacconi¹, Brijesh Purohit¹, Grand Ham¹, Tyler E Greenlee¹, Thais F D'Amico¹, Saraella Lofthouse-Gil¹, Mehmet Yasin Taka¹, Netai Choudhry¹, Adnan T Fung¹, Sabina Krasovic¹, Joon Baik¹, Ming Yan Lee¹, Vincent Suglione¹, Giuseppe Guimaraes¹, Erica Perini¹, Richard Rowan¹, Wen Ki Lee¹, Lawrence A Hernandez¹, Dinesh Sur¹, Anil Laxmavaran¹, Daniel Hauschildt¹, Harsh Singh¹, Nisha Sood¹, Jean Pierre Hubelshman¹, Michael Ip¹, Sothira Sooda¹, et Bailey Freund¹, David Sarraf¹



Multicenter Study | J Clin Ophthalmol. 2021 Mar;105(3):374-380.
doi: 10.1097/Ophth.0000000000000543. Epub 2020 May 6.

Henle fibre layer haemorrhage: clinical features and pathogenesis

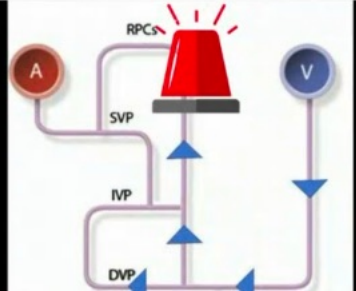
Caroline R Baumal¹, David Sarraf², Tara Bryant³, Wei Gu⁴, Nora Mukhtasov⁵, Francesco Rubi⁶, Giuseppe Quercqua⁷, Netai Choudhry⁸, Mehmet Yasin Taka⁹, Andrea Govetto¹⁰, Alessandro Invernizzi¹¹, Dean Elton¹², Aditi Gaudin¹³, Eduardo Cunha de Saiva¹⁴, Jonathan Noyman¹⁵, Andrea Limbo¹⁶, Grace C Lee¹⁷, K Bailey Freund¹⁸

Comparative Study | J Ophthalmol. 2019 Sep;30(9):156-166.
doi: 10.1097/OPT.0000000000000543. Epub 2019 Apr 10.

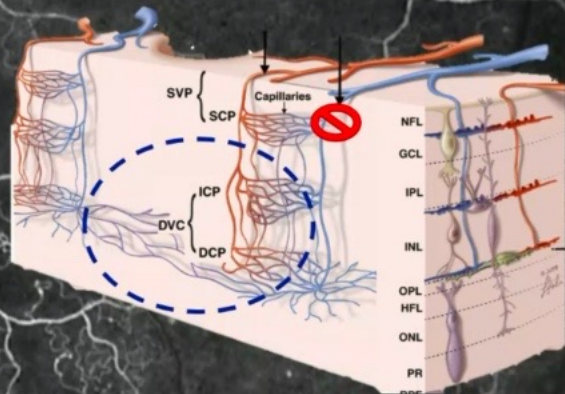
Impact and Implication of Fovea-Involving Intraretinal Hemorrhage after Acute Branch Retinal Vein Occlusion

James H Powers¹, Akshay S Thomas², Tahereh A Mir³, Jane S Kim⁴, Farib A Bimboone⁵, Stephen P Yoon⁶, Kim Khai⁷, Maria Gomez-Caraballo⁸, Shapiro Finkel⁹

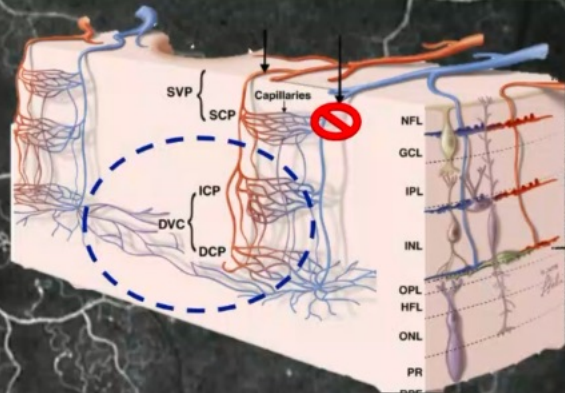
Higher hydrostatic pressure



COLLATERALS



COLLATERALS



Association of Optical Coherence Tomography Angiography of Collaterals in Retinal Vein Occlusion With Major Venous Outflow Through the Deep Vascular Complex

K Bailey Freund^{1,2}, David Sarraf^{3,4}, Belinda C S Leong¹, Sean Thomas Garrity³, Kiran K Vuppalapati¹

Affiliations +

Collateral Vessels in Branch Retinal Vein Occlusion: Anatomic and Functional Analyses by OCT Angiography



Kotaro Tsuboi¹, Hirofumi Sasajima², Motohiro Kamei²

Affiliations + expand

PMID: 31167790 DOI: 10.1016/j.ophtha.2019.04.015

Collateral Vessel Development in Central and Branch Retinal Vein Occlusions Are Associated With Worse Visual and Anatomic Outcomes



Alessandro Arrigo¹, Emanuela Aragona¹, Rosangela Lattanzio¹, Giovanni Scalia¹, Francesco Bandello¹, Maurizio Battaglia Parodi¹

Affiliations + expand

- Worse baseline and final VA
- Greater ischemia
- Greater ME severity
- More anti-VEGF injections

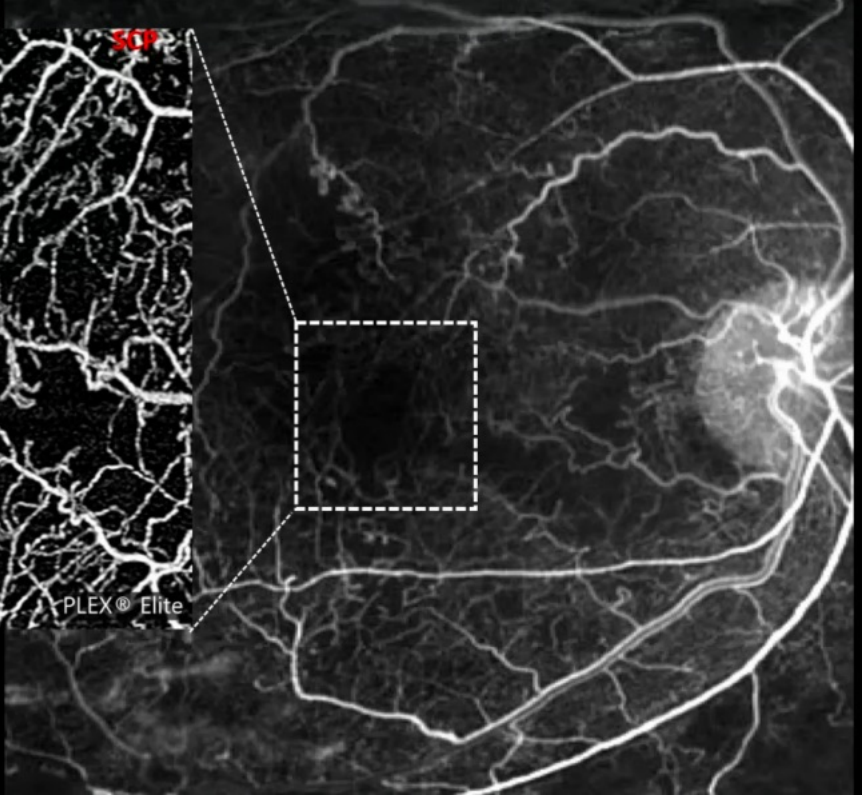
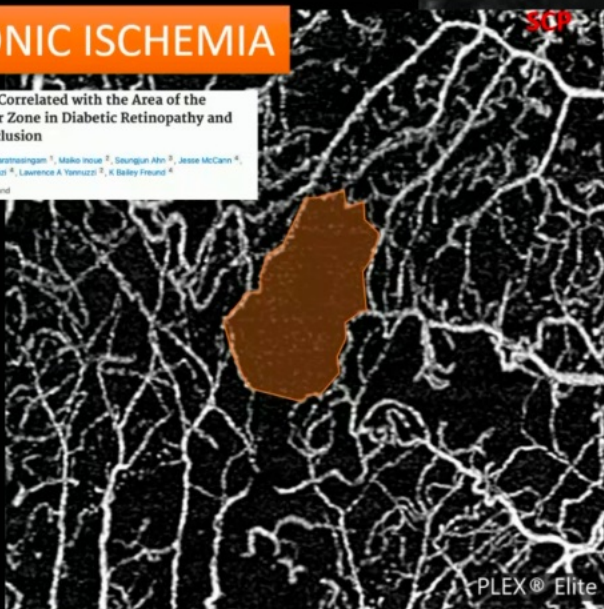
CHRONIC ISCHEMIA

Visual Acuity Is Correlated with the Area of the Foveal Avascular Zone in Diabetic Retinopathy and Retinal Vein Occlusion



Chandrakumar Balakrishnan¹, Meko Inoue², Seungun Ahn³, Jesse McCann⁴,
Elona Dhirani-Gavazi⁴, Lawrence A Yamuzzi², K Bailey Freund⁴

Affiliations [+ expand](#)



CHRONIC ISCHEMIA

Visual Acuity Is Correlated with the Area of the Foveal Avascular Zone in Diabetic Retinopathy and Retinal Vein Occlusion



Chendrakumar Balasubramanian¹, Meko Inoue², Seungun Ahn³, Jesse McCann⁴, Elona Dhirani-Gaucci⁴, Lawrence A Yonuzzi², K Bailey Freund⁴

Affiliations + expand

DCP

Worse baseline VA

Persistent/recurrent ME

Peripheral non-perfusion

CORRELATION OF MICROVASCULAR STRUCTURES ON OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY WITH VISUAL ACUITY IN RETINAL VEIN OCCLUSION



Joon-Won Kang¹, Romi Yoo, Youn Hye Jo, Hyung Chan Kim

Affiliations + expand

PMID: 27828907 DOI: 10.1097/AE.0000000000001403

GAP IN CAPILLARY PERFUSION AND BURDEN OF TREATMENT IN BRANCH RETINAL VEIN OCCLUSION: A Wide-Field Optical Coherence Tomography Angiography Study



Kunho Sae¹, Seu-Ki Bang², Se Woong Kang³, Eung Suk Kim², Seung-Young Yu²

Affiliations + expand

PMID: 33149096 DOI: 10.1097/AE.0000000000003006

Deep Capillary Plexus as Biomarker of Peripheral Capillary Nonperfusion in Central Retinal Vein Occlusion



Maurizio Battaglia Parodi¹, Alessandro Arrigo¹, Alessio Antropoli¹, Lorenzo Bianco¹, Andrea Saladino¹, Francesco Benedello¹, Manuel Vilela², Ahmed Mansour³

Affiliations + expand

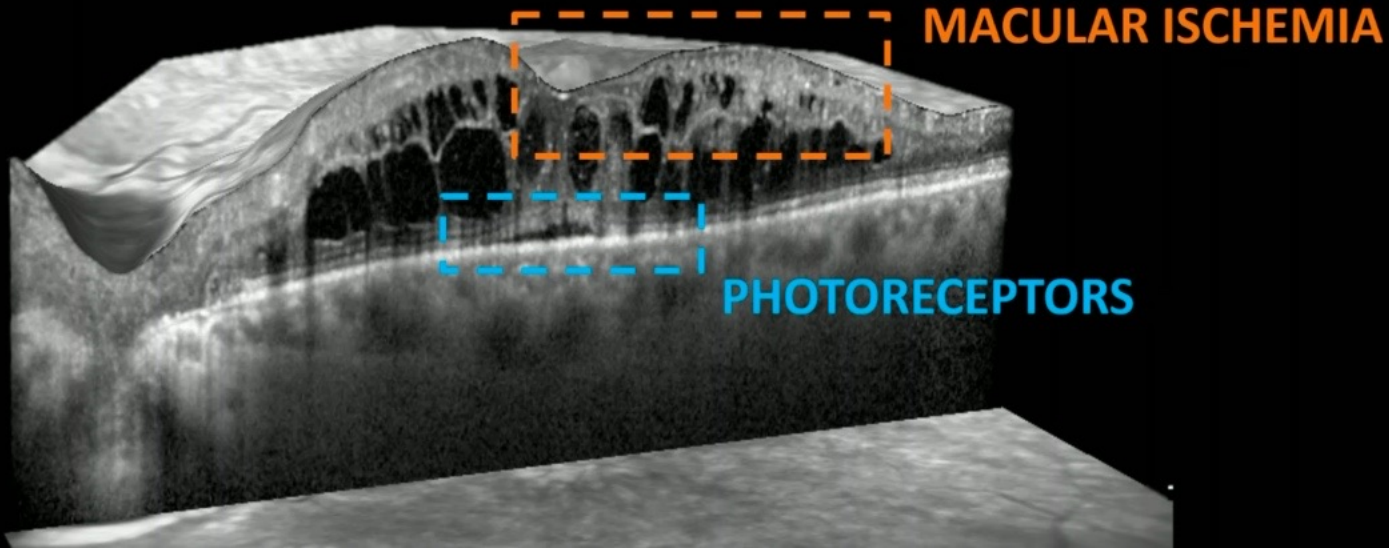
PMID: 36824600 PMID: PMC941371 DOI: 10.1016/j.eyes.2022.100267

The impact of structural optical coherence tomography changes on visual function in retinal vein occlusion



Martin Michl¹, Xuhui Liu^{1, 2}, Alexandra Kaider³, Amir Sadeghipour¹,
Blanca S Gerendas¹, Ursula Schmidt-Erfurth¹

Affiliations + expand



PHOTORECEPTORS

Randomized Controlled Trial | Ophthalmol Retina. 2021 Nov;5(11):1115-1124.
doi: 10.1016/j.oret.2021.02.004. Epub 2021 Feb 19.

Predictors of Visual Acuity Outcomes after Anti-Vascular Endothelial Growth Factor Treatment for Macular Edema Secondary to Central Retinal Vein Occlusion



Piyali Sen¹, Sreerag Gurudas², Jayashree Ramu³, Namritha Patrao³,
Shruti Chandra¹, Rajni Rasheed³, Luke Nicholson³, Tunde Peto³,
Sobha Sivasubramanian³, Philip Hykin¹

Clinical Trial | Ophthalmol Retina. 2021 Oct;5(10):991-998. doi: 10.1016/j.oret.2020.12.016.
Epub 2020 Dec 26.

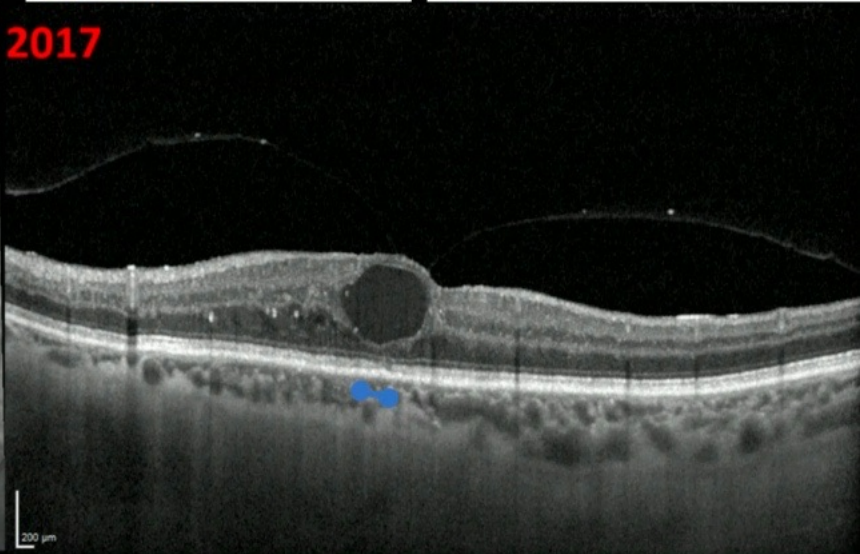
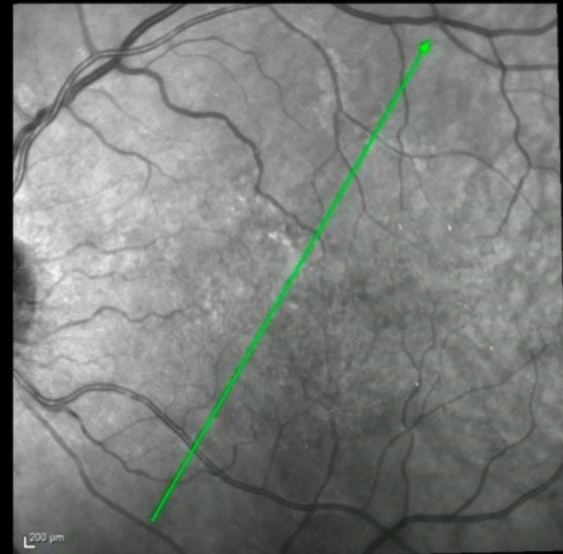
Spectral Domain OCT Predictors of Visual Acuity in the Study of Comparative Treatments for Retinal Vein Occlusion 2: SCORE 2 Report 15



Tyler Etheridge¹, Barbara Blodi¹, Neal Oden², Paul Van Veldhuisen²,
Ingrid U Scott³, Michael S Ip⁴, Mihai Mitoku⁵, Amitha Domalpally⁵

Affiliations + expand

2017



PHOTORECEPTORS

Randomized Controlled Trial | Ophthalmol Retina. 2021 Nov;5(11):1115-1124.
doi: 10.1016/j.oret.2021.02.004. | pub 2021 Feb 19.

Predictors of Visual Acuity Outcomes after Anti-Vascular Endothelial Growth Factor Treatment for Macular Edema Secondary to Central Retinal Vein Occlusion



Riyal Sen ¹, Sreega Gurudas ², Jayashree Ramu ³, Namritha Patrao ³,
Shruti Chandra ³, Rajna Rasheed ³, Luke Nicholson ³, Tunde Peto ³,
Sobha Sivaprasad ³, Philip Hykin ¹

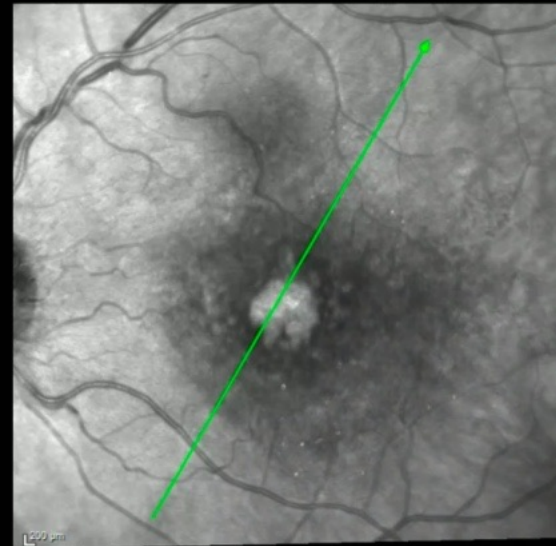
Clinical Trial | Ophthalmol Retina. 2021 Oct;5(10):991-998. doi: 10.1016/j.oret.2020.12.016.
Epub 2020 Dec 26.

Spectral Domain OCT Predictors of Visual Acuity in the Study of Comparative Treatments for Retinal Vein Occlusion 2: SCORE 2 Report 15

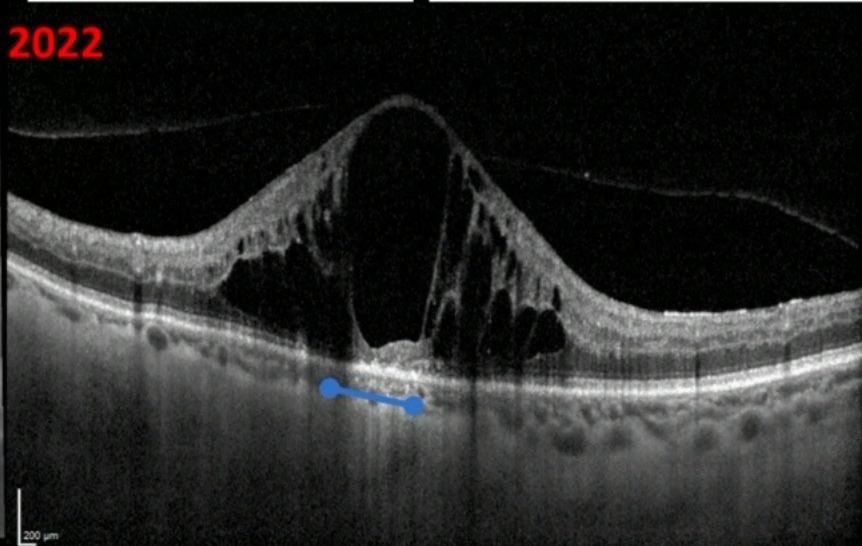


Tyler Etheridge ¹, Barbara Blodi ¹, Neal Oden ², Paul Van Veldhuisen ²,
Ingrid U Scott ³, Michael S Ip ⁴, Mihai Mitescu ¹, Amritha Domalpally ⁵

Affiliations + expand



2022



PHOTORECEPTORS

Randomized Controlled Trial | Ophthalmol Retina. 2021 Nov;5(11):1115-1124.
doi: 10.1016/j.oret.2021.02.008. (pub 2021 Feb 19)

Predictors of Visual Acuity Outcomes after Anti-Vascular Endothelial Growth Factor Treatment for Macular Edema Secondary to Central Retinal Vein Occlusion



Riyal Sen ¹, Sreya Gurudas ², Jayashree Ramu ³, Namritha Patrao ³,
Shruti Chandra ¹, Raju Rasheed ², Luke Nicholson ³, Tunde Peto ³,
Sobha Sivasubramanian ¹, Philip Hykin ¹

Clinical Trial | Ophthalmol Retina. 2021 Oct;5(10):991-998. doi: 10.1016/j.oret.2020.12.016.
Epub 2020 Dec 26.

Spectral Domain OCT Predictors of Visual Acuity in the Study of Comparative Treatments for Retinal Vein Occlusion 2: SCORE 2 Report 15

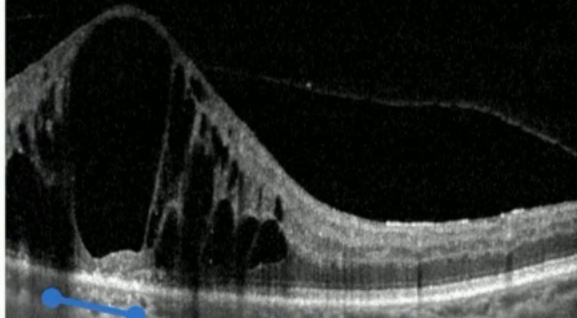
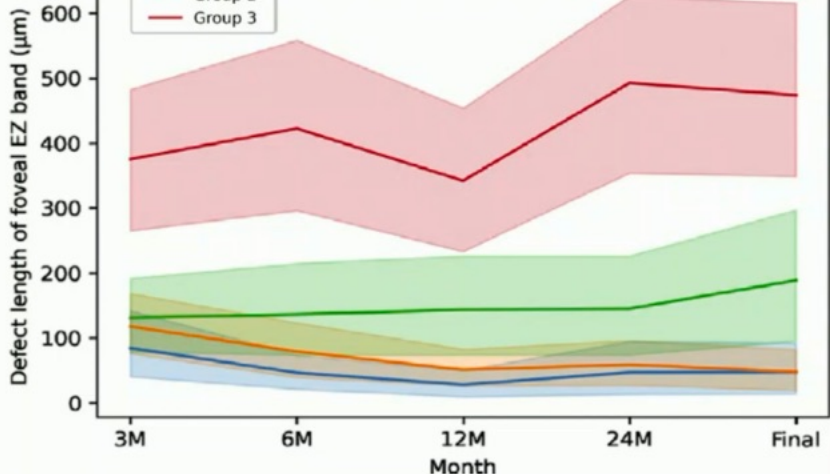


Tyler Etheridge ¹, Barbara Blodi ¹, Neal Oden ², Paul Van Veldhuisen ²,
Ingrid U Scott ³, Michael S Ip ⁴, Mihai Mitteleu ¹, Armitha Domalpally ⁵

Affiliations + expand

Foveal thickness fluctuation

— Group 0
— Group 1
— Group 2
— Group 3



Observational Study | Ophthalmol Retina. 2020 Dec;4(12):1158-1169.

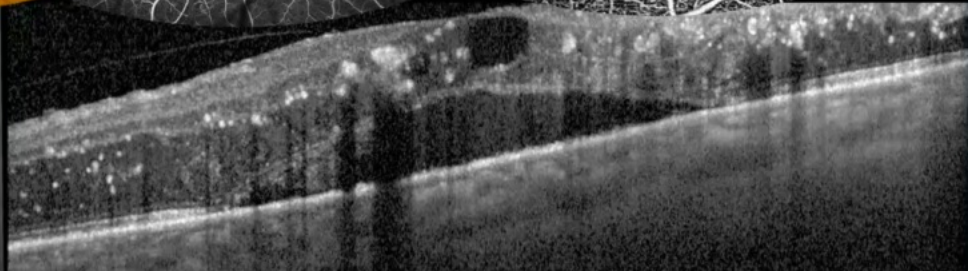
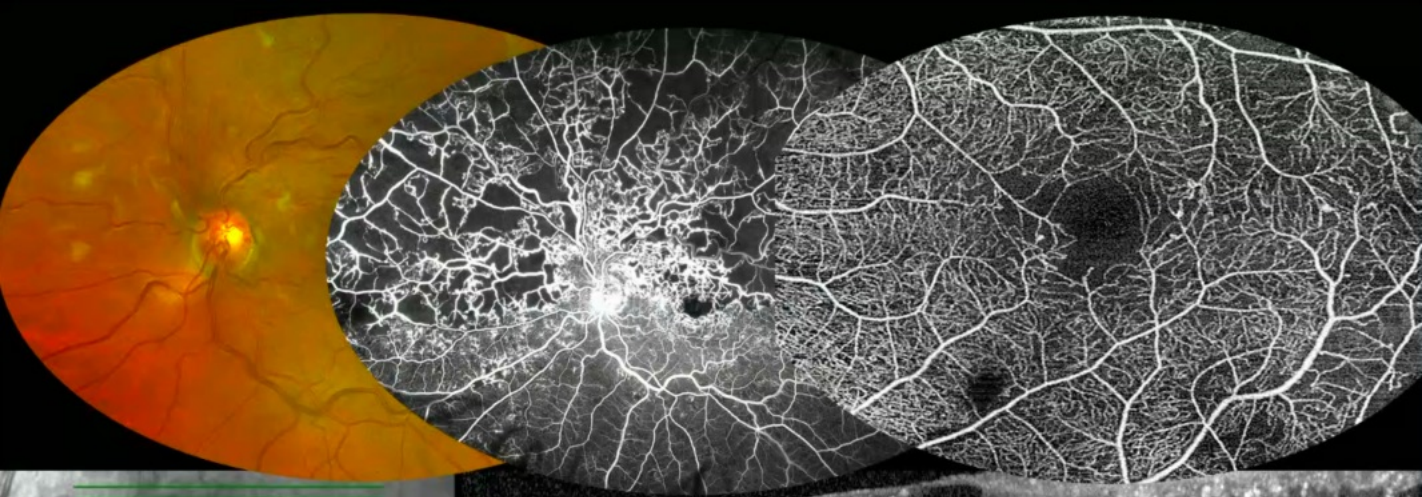
doi: 10.1016/j.oret.2020.05.018. Epub 2020 May 29.

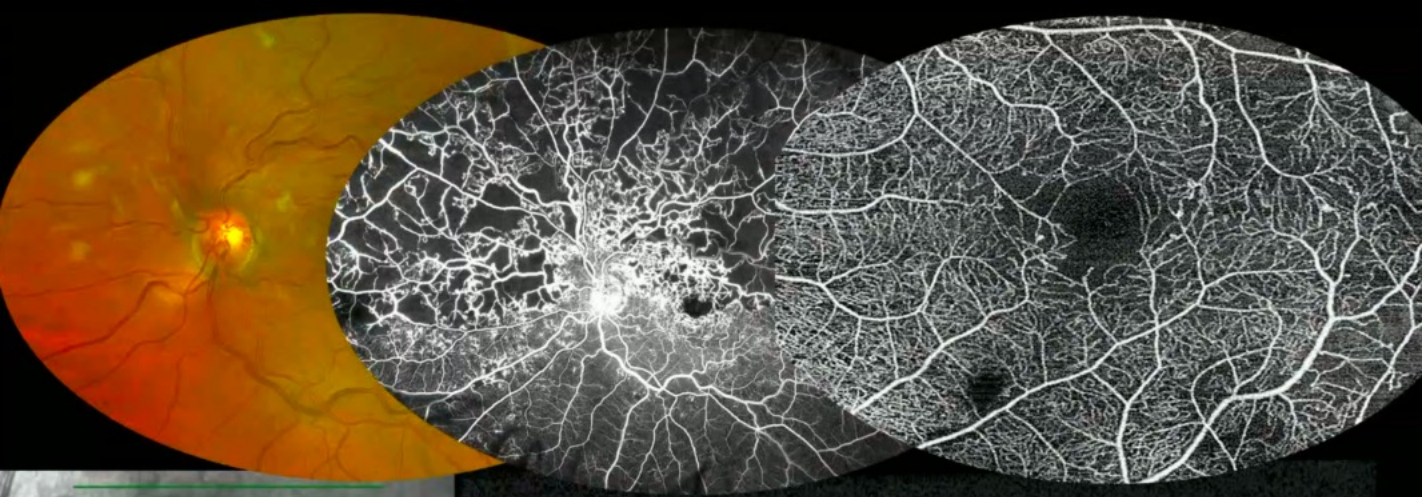
Fluctuations in Macular Thickness in Patients with Retinal Vein Occlusion Treated with Anti-Vascular Endothelial Growth Factors



Andrew X Chen ¹, Tyler E Greenlee ², Thais F Conti ², Isaac N Briskin ³,
Rishi P Singh ⁴

Affiliations + expand





Anti-VEGF: randomized trials

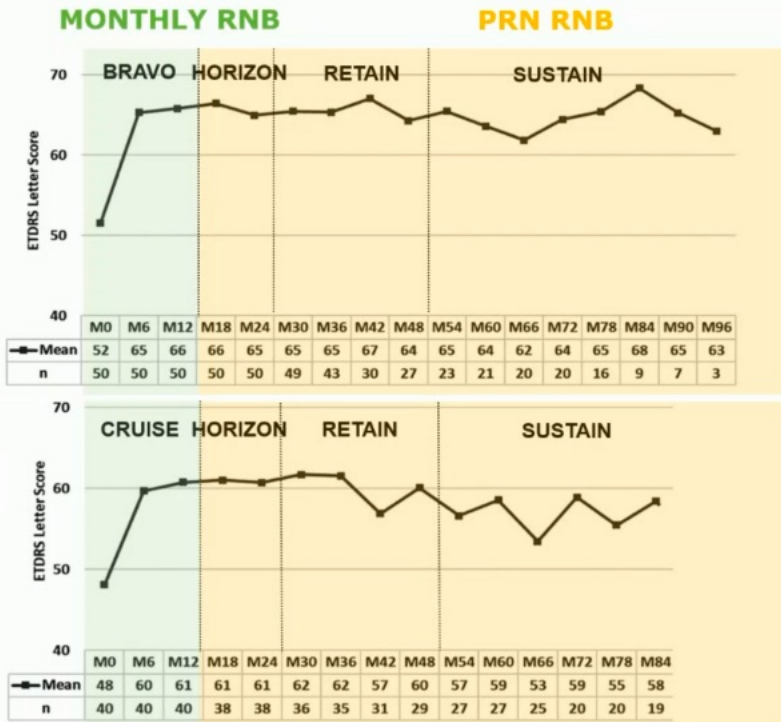
Clinical Trial > Ophthalmology. 2014 Jan;121(1):209-219. doi: 10.1016/j.ophtha.2013.08.038.
Epub 2013 Oct 7.

Long-term outcomes in patients with retinal vein occlusion treated with ranibizumab: the RETAIN study



Peter A Campochiaro¹, Raafay Sophie², Joel Pearlman³, David M Brown⁴,
David S Boyer⁵, Jeffrey S Heier⁶, Dennis M Marcus⁷, Leonard Feiner⁸,
Arun Patel³; RETAIN Study Group

0.5 mg PRN ranibizumab at **7 years**

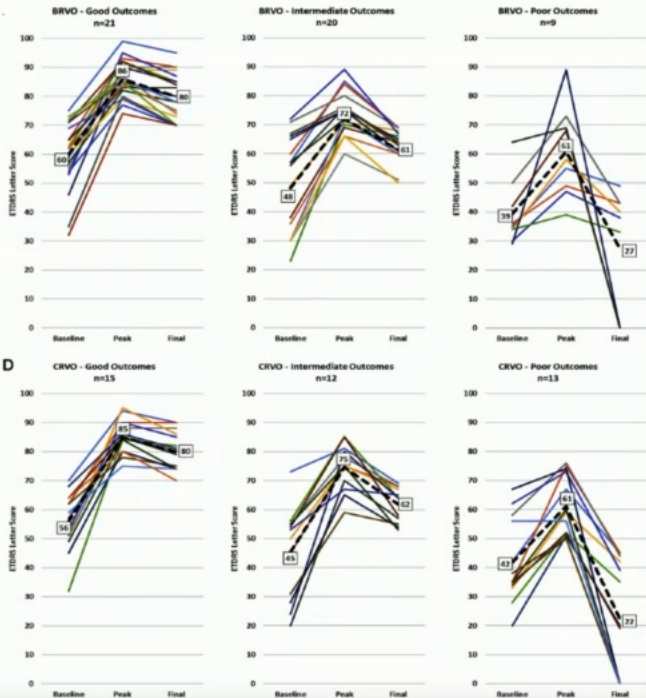


Loss of Peak Vision in Retinal Vein Occlusion Patients Treated for Macular Edema



Mustafa Iftikhar ¹, Tahreem A Mir ¹, Gulnar Hafiz ¹, Ingrid Zimmer-Galler ¹,
Adrienne W Scott ¹, Sharon D Solomon ¹, Akrit Sodhi ¹, Adam S Wenick ¹,
Catherine Meyerle ¹, Kim Jiramongkolchai ¹, T Y Alvin Liu ¹, J Fernando Arevalo ¹,
Mandeep Singh ¹, Saleema Kherani ¹, James T Handa ¹, Peter A Campochiaro ²

Single-eye trajectories in CRUISE, BRAVO,
HORIZON, RETAIN, RELATE extended
follow-up



Loss of Peak Vision in Retinal Vein Occlusion Patients Treated for Macular Edema

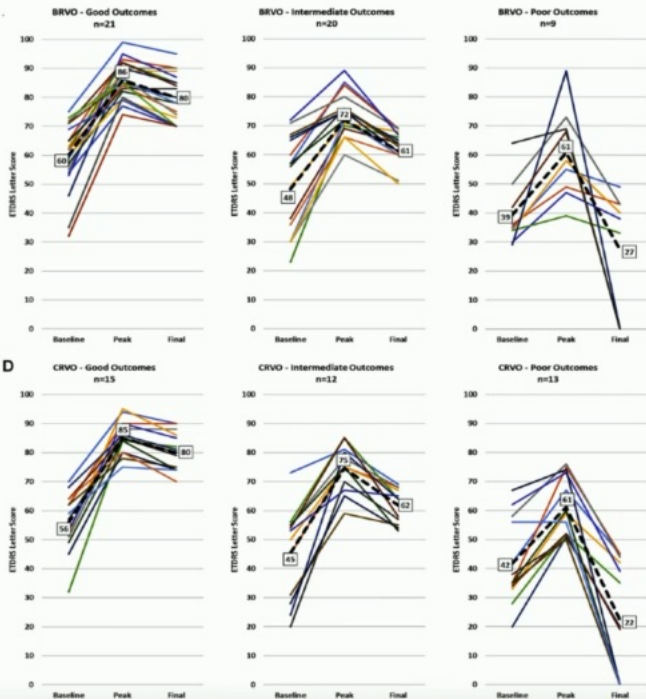


Mustafa Iftikhar ¹, Tahreem A Mir ¹, Gulnar Hafiz ¹, Ingrid Zimmer-Galler ¹,
Adrienne W Scott ¹, Sharon D Solomon ¹, Akrit Sodhi ¹, Adam S Wenick ¹,
Catherine Meyerle ¹, Kim Jiramongkolchai ¹, T Y Alvin Liu ¹, J Fernando Arevalo ¹,
Mandeep Singh ¹, Saleema Kherani ¹, James T Handa ¹, Peter A Campochiaro ²

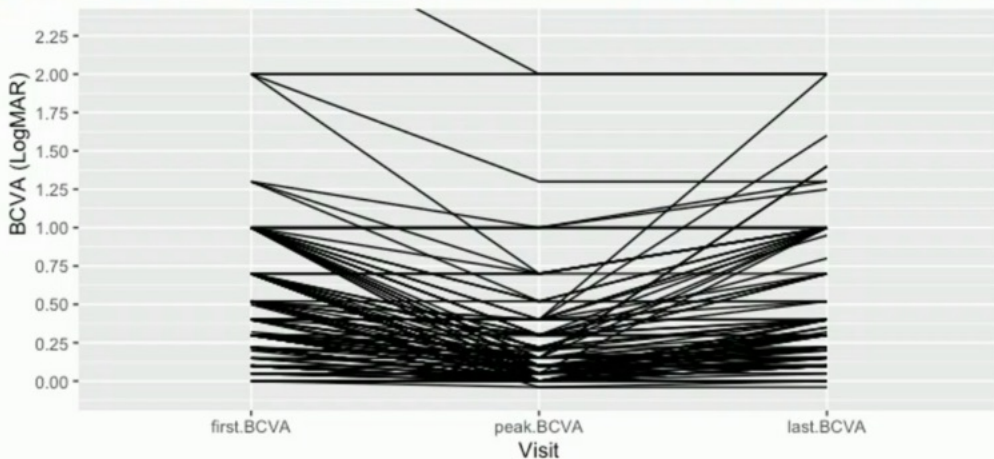
Single-eye trajectories in CRUISE, BRAVO,
HORIZON, RETAIN, RELATE extended
follow-up



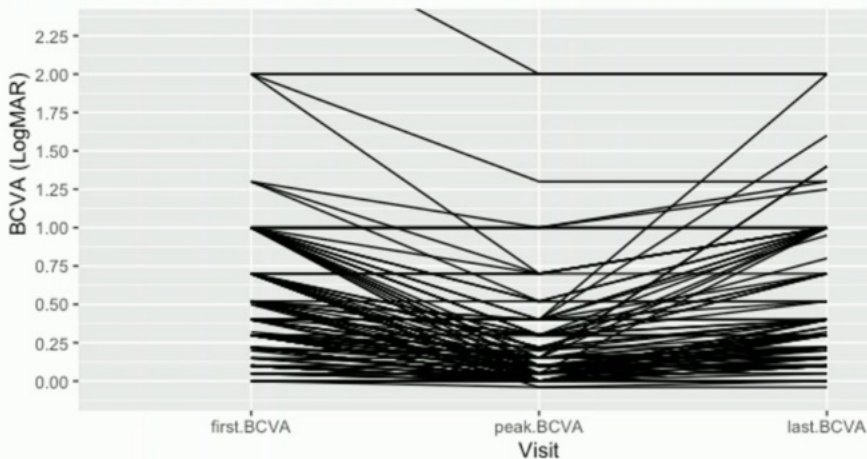
PEAK VISION LOSS



Real-life data (213 naïve RVO eyes)



Real-life data (213 naïve RVO eyes)



IMPACT OF RETINAL ISCHEMIA ON FUNCTIONAL AND ANATOMICAL OUTCOMES AFTER ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY IN PATIENTS WITH RETINAL VEIN OCCLUSION



Melaad Khayat^{1,2}, David M Wright³, Jiantee Yeong⁴, Daniel Xu¹, Christopher Donley³, Gokul R Lakshminpathy³, Mei Ken Low³, Natasha White³, Michael Williams^{4,5}, Noemi Lois^{1,4}

PERIPHERAL ISCHEMIA

Clinical Trial > Ophthalmol Retina. 2018 Feb;2(2):134-142. doi: 10.1016/j.oret.2017.05.016. Epub 2017 Sep 9.

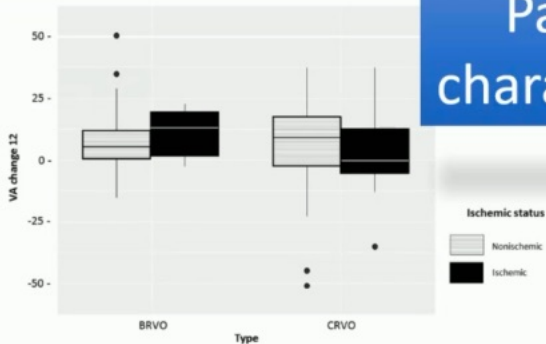
Sustained Benefits from Ranibizumab for Central Retinal Vein Occlusion with Macular Edema: 24-Month Results of the CRYSTAL Study



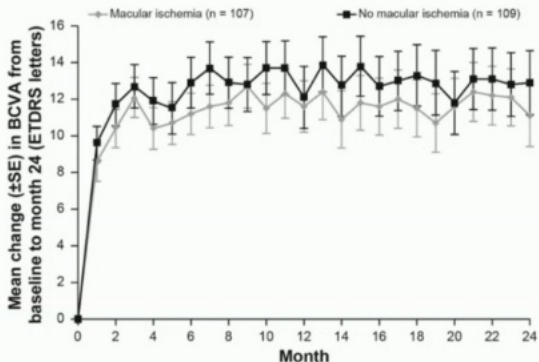
Michael Larsen¹, Sebastian M Waldstein², Siegfried Priglinger³, Philip Hykin⁴, Elizabeth Barnes⁵, Margarita Gekkieva⁵, Ayan Das Gupta⁶, Andreas Wenzel⁵, Jordi Monés⁷; CRYSTAL Study Group

MACULAR ISCHEMIA

Visual acuity change at 12-month follow-up [ETDRS letters]



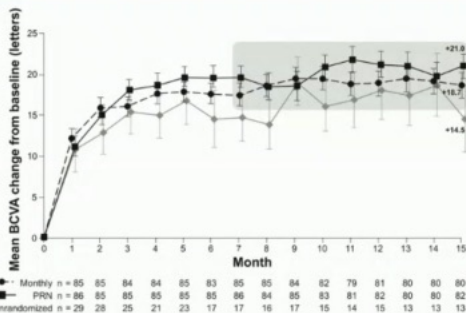
Patients' characteristics



Monthly versus as-needed ranibizumab injections in patients with retinal vein occlusion: the SHORE study

Peter A Campochiaro¹, Charles C Wyckoff², Michael Singer³, Robert Johnson⁴, Dennis Marcus⁵, Linda Yau⁶, Gary Sternberg⁶

Affiliations + expand



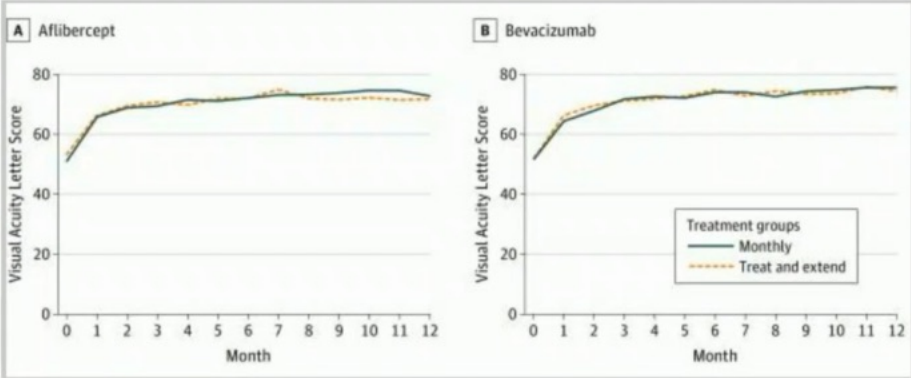
Treatment regimen

FIXED=PRN

Comparison of Monthly vs Treat-and-Extend Regimens for Individuals With Macular Edema Who Respond Well to Anti-Vascular Endothelial Growth Factor Medications: Secondary Outcomes From the SCORE2 Randomized Clinical Trial

Ingrid U Scott^{1,2}, Paul C VanVeldhuisen³, Michael S Ip⁴, Barbara A Blodi⁵, Neal L Oden³, Michael Altaweel⁶, Daniel M Berenstein⁷; SCORE2 Investigator Group

Affiliations + expand



FIXED=T&E

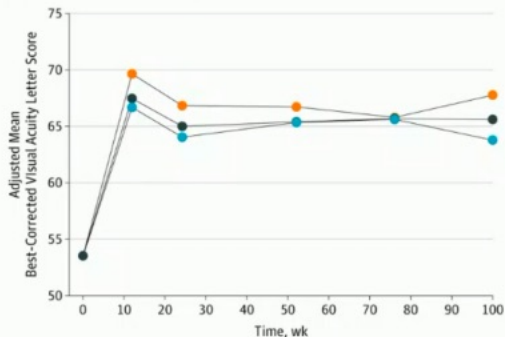
Clinical Effectiveness of Intravitreal Therapy With Ranibizumab vs Aflibercept vs Bevacizumab for Macular Edema Secondary to Central Retinal Vein Occlusion: A Randomized Clinical Trial



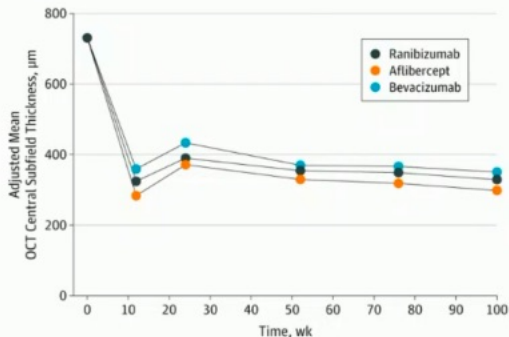
Philip Hykin¹, A Toby Prevost², Joana C Vasconcelos², Caroline Murphy³,
Joanna Kelly³, Jayashree Ramu¹, Barry Hounsome³, Yit Yang⁴, Simon P Harding⁵,
Andrew Lotery⁶, Usha Chakravarthy⁷, Sobha Sivaprasad¹; LEAVO Study Group

Treatment agent

A Best-corrected visual acuity



B Adjusted mean optical coherence tomography (OCT) central subfield thickness



Aflibercept = Ranibizumab = Bevacizumab

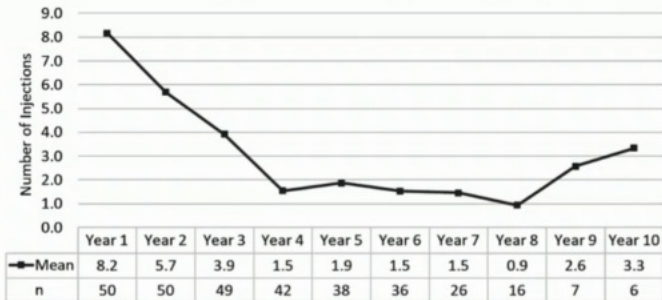
Loss of Peak Vision in Retinal Vein Occlusion Patients Treated for Macular Edema



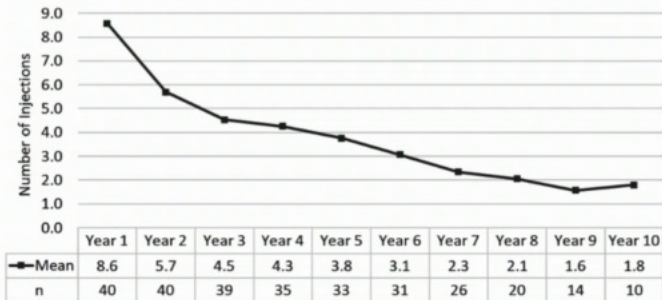
Mustafa Iftikhar ¹, Tahreem A Mir ¹, Gulnar Hafiz ¹, Ingrid Zimmer-Galler ¹,
Adrienne W Scott ¹, Sharon D Solomon ¹, Akrit Sodhi ¹, Adam S Wenick ¹,
Catherine Meyerle ¹, Kim Jiramongkolchai ¹, T Y Alvin Liu ¹, J Fernando Arevalo ¹,
Mandeep Singh ¹, Saleema Kherani ¹, James T Handa ¹, Peter A Campochiaro ²



BRVO - Mean Number of Intravitreal Anti-VEGF Injections



CRVO - Mean Number of Intravitreal Anti-VEGF Injections



Loss of Peak Vision in Retinal Vein Occlusion Patients Treated for Macular Edema

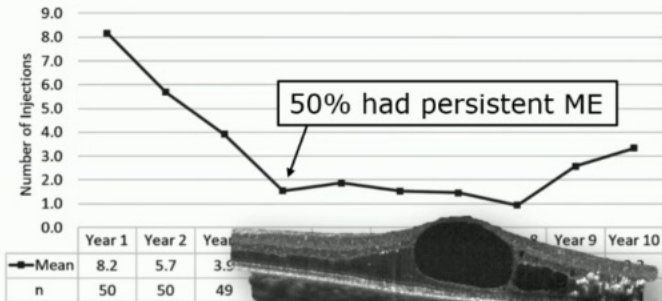


Mustafa Iftikhar¹, Tahreem A Mir¹, Gulnar Hafiz¹, Ingrid Zimmer-Galler¹,
Adrienne W Scott¹, Sharon D Solomon¹, Akrit Sodhi¹, Adam S Wenick¹,
Catherine Meyerle¹, Kim Jiramongkolchai¹, T Y Alvin Liu¹, J Fernando Arevalo¹,
Mandeep Singh¹, Saleema Kherani¹, James T Handa¹, Peter A Campochiaro²

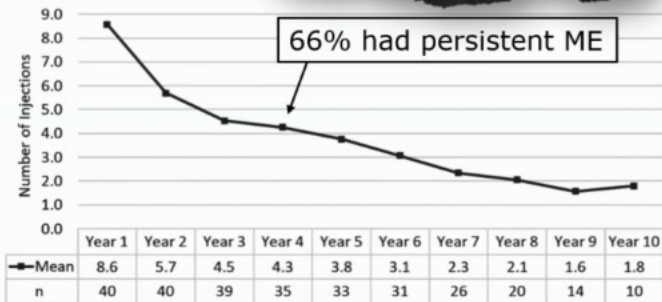


UNDERTREATMENT

BRVO - Mean Number of Intravitreal Anti-VEGF Injections



CRVO - Mean Number of Intravitreal Anti-VEGF Injections



Central Retinal Vein Occlusion 36-Month Outcomes with Anti-VEGF: The Fight Retinal Blindness! Registry



Adrian Hunt¹, Vuong Nguyen², Sanjeeb Bhandari³, Theodorus Ponsioen⁴, Ian L McAllister⁵, Jennifer Arnold⁶, Stephanie Young⁷, Pierre-Henry Gabrielle⁸, Hemal Mehta⁹, Louise O' Toole¹⁰, Socorro Alforja¹¹, Javier Zarranz-Ventura¹¹, Daniel Barthelmes¹², Mark Gillies²

- Erosion of VA gains from 2 to 36 months
- 12% eyes achieved ME resolution

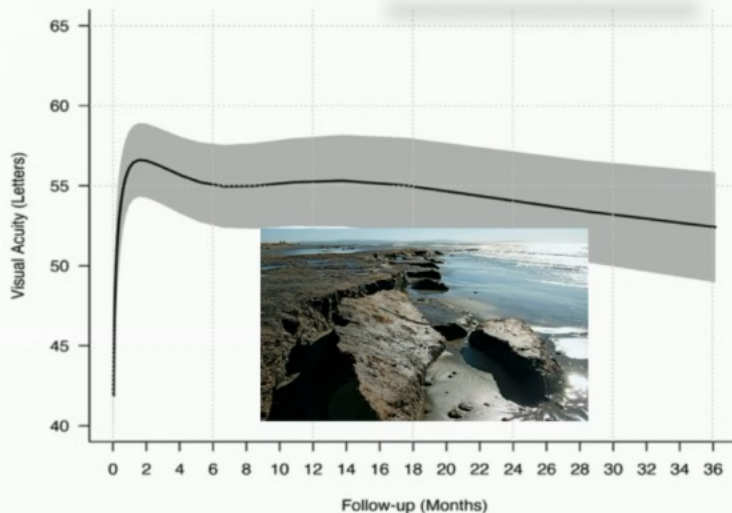
Randomized Controlled Trial > Eye (Lond). 2022 Aug;36(8):1656-1661.

doi: 10.1038/s41433-021-01702-y. Epub 2021 Jul 29.

Effectiveness and safety of ranibizumab in patients with central retinal vein occlusion: results from the real-world, global, LUMINOUS study



Andrew Lotery¹, Andreas Clemens^{2,3}, Raman Tuli⁴, Xun Xu⁵, Masahiko Shimura⁶, Marco Nardi⁷, Focke Ziemssen⁸, Cornelia Dunger-Baldauf⁹, Ramin Tadayoni¹⁰; LUMINOUS™ study group



Central Retinal Vein Occlusion 36-Month Outcomes with Anti-VEGF: The Fight Retinal Blindness! Registry



Adrian Hunt¹, Vuong Nguyen², Sanjeeb Bhandari³, Theodorus Ponsoen⁴, Ian L McAllister⁵, Jennifer Arnold⁶, Stephanie Young⁷, Pierre-Henry Gabrielle⁸, Hemal Mehta⁹, Louise O' Toole¹⁰, Socorro Alforja¹¹, Javier Zarranz-Ventura¹¹, Daniel Barthelmes¹², Mark Gillies²

- Erosion of VA gains from 2 to 36 months
- 12% eyes achieved ME resolution

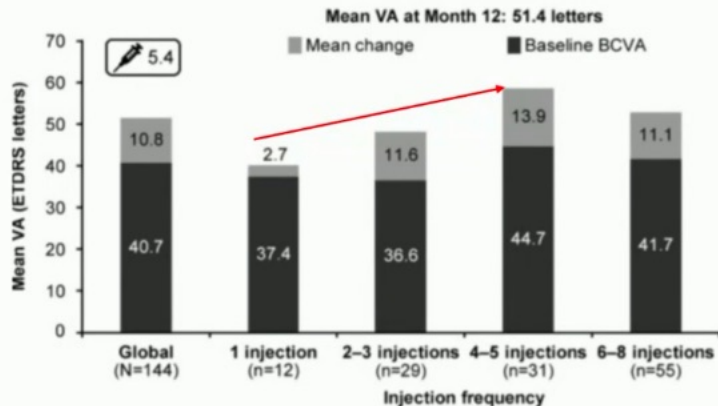
Randomized Controlled Trial > Eye (Lond). 2022 Aug;36(8):1656-1661.

doi: 10.1038/s41433-021-01702-y. Epub 2021 Jul 29.

Effectiveness and safety of ranibizumab in patients with central retinal vein occlusion: results from the real-world, global, LUMINOUS study



Andrew Lotery¹, Andreas Clemens^{2,3}, Raman Tuli⁴, Xun Xu⁵, Masahiko Shimura⁶, Marco Nardi⁷, Focke Ziemssen⁸, Cornelia Dunger-Baldauf⁹, Ramin Tadayoni¹⁰; LUMINOUS™ study group



TAKE HOME MESSAGES

- Good immediate response, but **vision loss** in the long-term
- Considerable rate of **persistent/recurrent ME** at 3 years
- Individualized dosing (fixed, proactive) or alternative drugs in non-responding patients



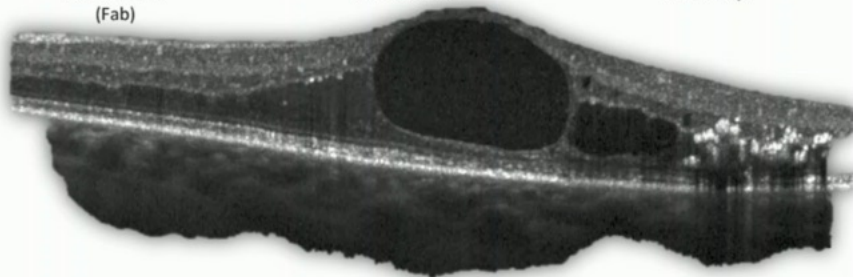
Ranibizumab
(Fab)



Bevacizumab

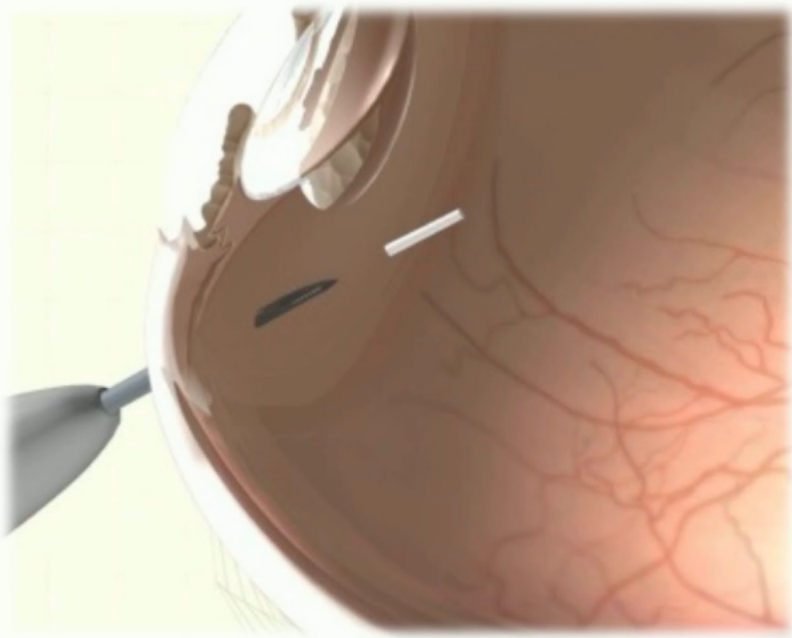


Aflibercept



TAKE HOME MESSAGES

- Good immediate response, but vision loss in the long-term
- Considerable rate of persistent/recurrent ME at 3 years
- **Individualized dosing** (fixed, proactive) or **alternative drugs** in non-responding patients



Steroids for macular edema due to RVO

Sarah Touhami, MD-PhD

Associate Professor of Ophthalmology

CHU Pitié Salpêtrière

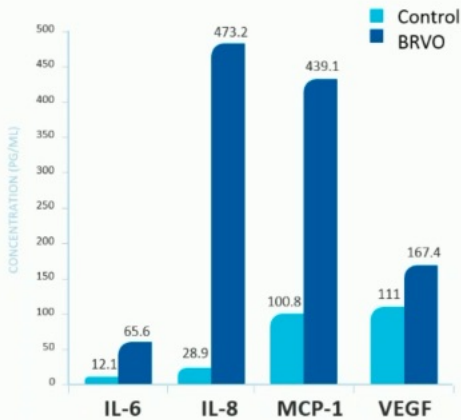
Paris, France

Steroids for macular edema in RVO

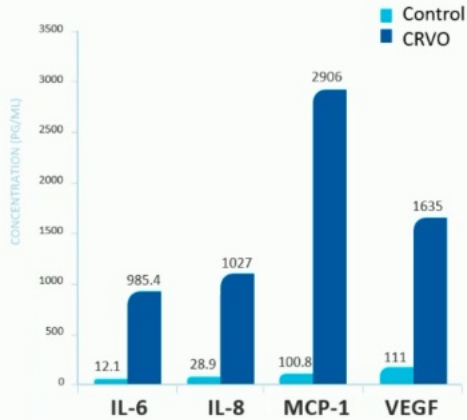
Inflammation

Overexpression of pro inflammatory cytokines

BRVO: Concentration in the vitreous

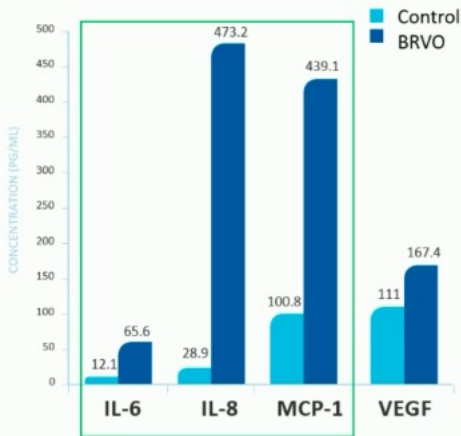


CRVO: Concentration in the vitreous

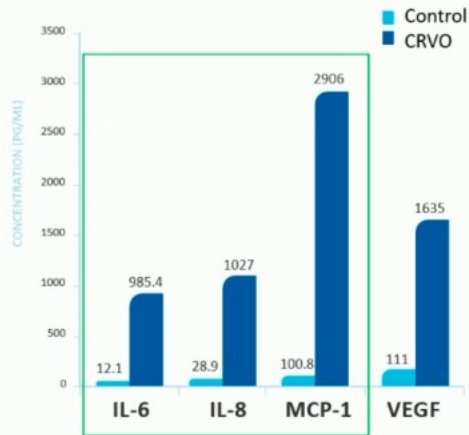


Overexpression of pro inflammatory cytokines

BRVO: Concentration in the vitreous



CRVO: Concentration in the vitreous



Macular edema treatment in RVO

DEXi

GENEVA

Reinjection interval **6 months**

16.4% of patients had an RVO < 3 months

COMO

Reinjection at **5 months** and 5-6 months later if necessary

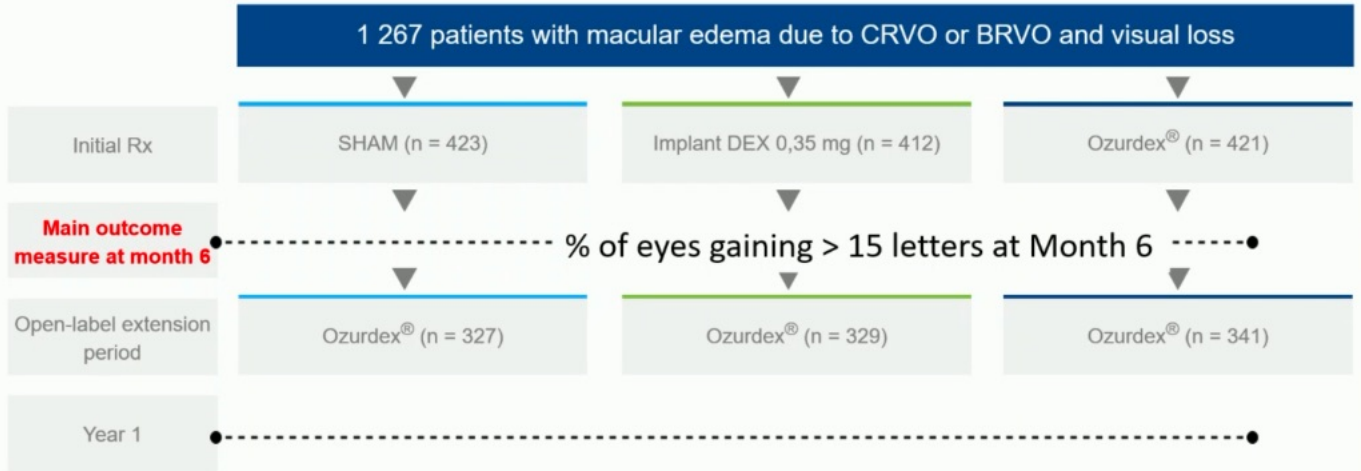
BRVO < 3 months

COBALT

Reinjection interval **4 months**

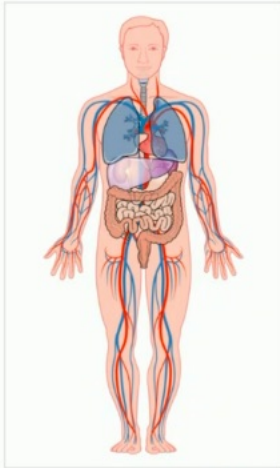
BRVO < 3 months

The GENEVA Randomized Clinical Trial



* Retreatment : BCVA < 84 letters ; CMT > 250 µm

Inclusion criteria



INCLUSION CRITERIA

Patients \geq 18 years

BCVA : 34 (20/200) to 68 (20/50)
ETDRS letters

Duration of macular edema :

- CRVO : 6 weeks to 9 months
 - BRVO : 6 weeks to 12 months
-

CMT \geq 300 μ m in the central 1 mm

Baseline Characteristics

	Ozurdex® n=427	Sham n=426
Mean age, years	64.7	63.9
Gender		
Male (%)	50.8	56.3
Diagnosis		
CRVO (%)	31.9	34.5
BRVO (%)	68.1	65.5
Macular edema duration		
Mean, days	157.6	156.1
< 90 days(%)	16.4	15.3
90-179 days (%)	51.3	51.6
≥ 180 days (%)	32.3	33.1
BCVA, mean ETDRS letters (Snellen)	54.3 (20/80)	54.8 (20/80)
CMT, μm	562.0	539
Ocular hypertension Rx (%)	6	4

Patients with macular edema < 3 months are more likely to gain vision^{1,2}

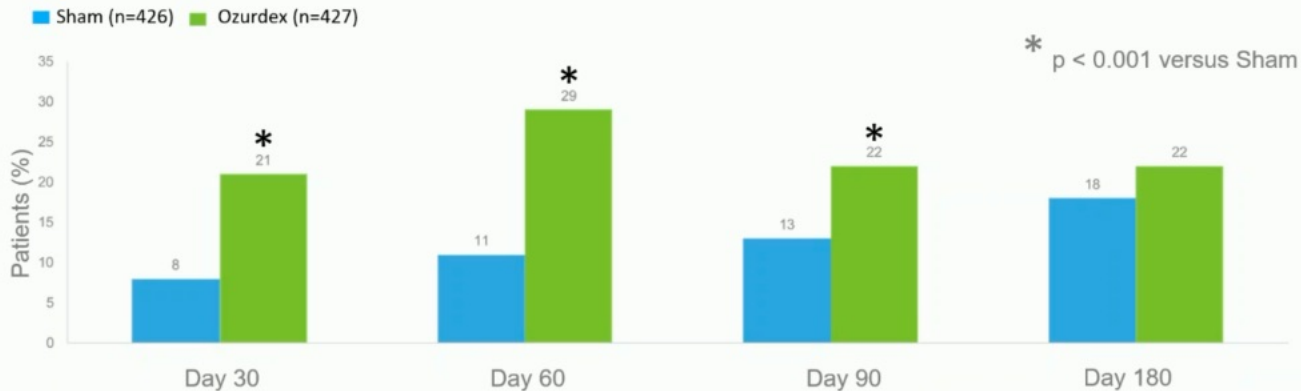
~85 % of patients had macular edema > 3 months, which may have affected the outcomes in the GENEVA trial

1. Haller JA, et al. Ophthalmology 2010;117:1134-48.

2. Scott IU, et al. Ophthalmology 2011;118:345-52.

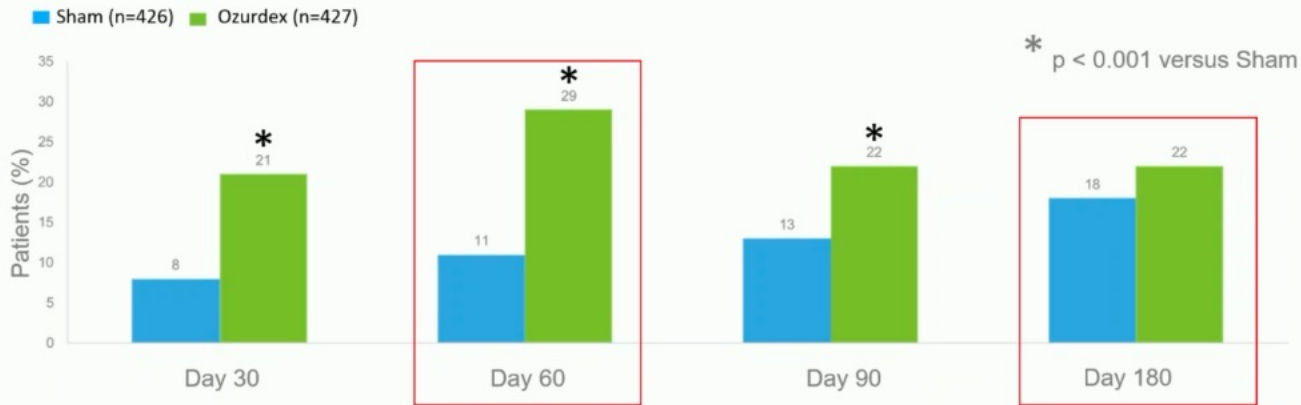
Main outcome : > 15-letter gainers at month 6

Ozurdex® allowed more patients to reach the outcome at 1, 2 and 3 months versus Sham

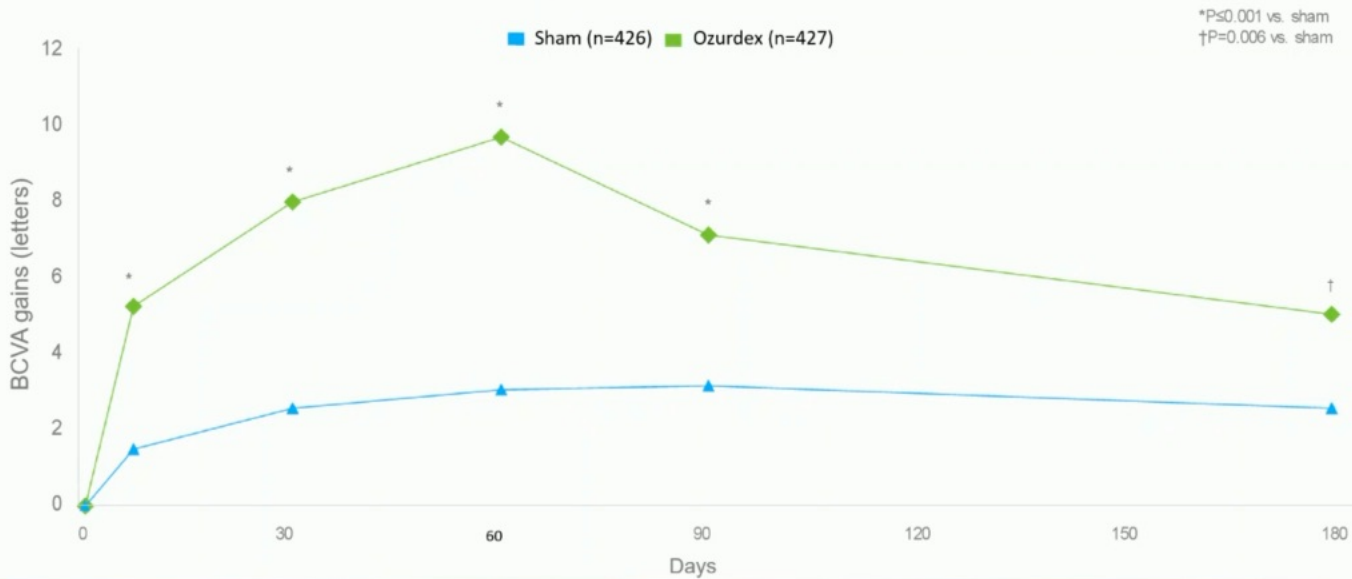


Main outcome : > 15-letter gainers at month 6

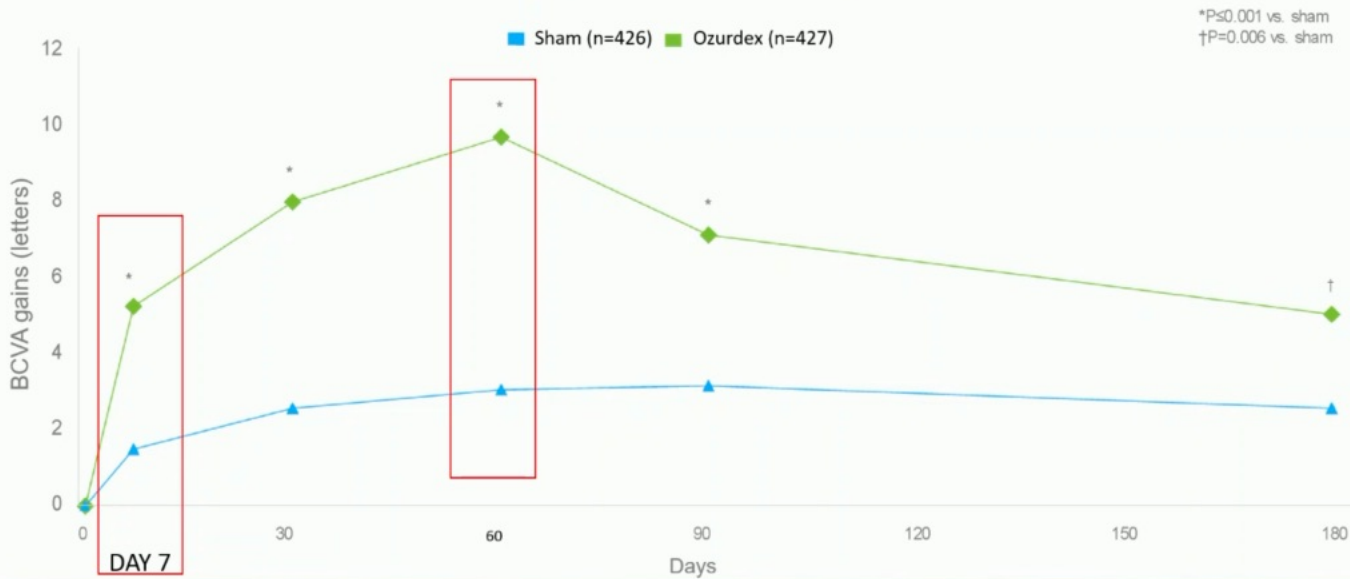
Ozurdex® allowed more patients to reach the outcome at 1, 2 and 3 months versus Sham



Rapid BCVA improvement



Rapid BCVA improvement



Secondary outcomes: CMT

CMT evolution after treatment



Secondary outcomes: CMT

CMT evolution after treatment



Early management leads to better BCVA outcomes

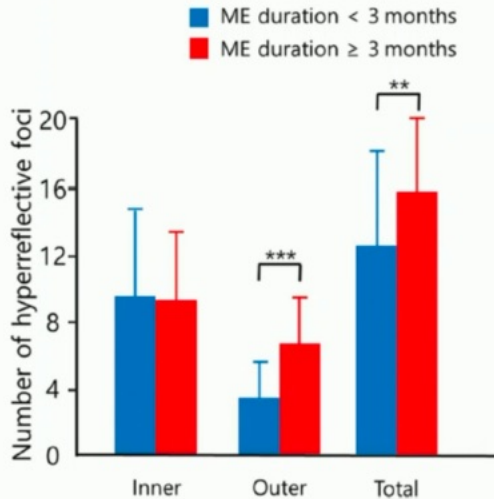
BCVA evolution



Real-life studies : Treatment naive macular edema ≥ 3 months

Do et al. Retina, 2020

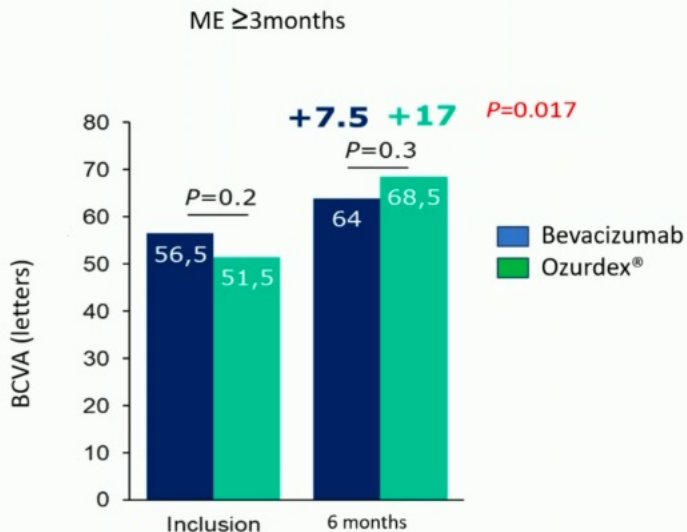
- Retrospective monocentric study
- 139 eyes of 139 patients
- BRVO with Rx naive macular edema
 - 69 eyes treated with bevacizumab (1 then PRN)
 - 70 eyes treated with DEX-i
- Higher N of HRF in the outer retina of BRVO eyes with ME ≥ 3 months
- Better BCVA gains with DEXi in eyes with ME ≥ 3 months: +17 vs. +7.5 letters ($p=0.017$)
 - Better HRF resolution with DEXi ($p<0.001$)



Real-life studies : Treatment naive macular edema ≥ 3 months

Do et al. Retina, 2020

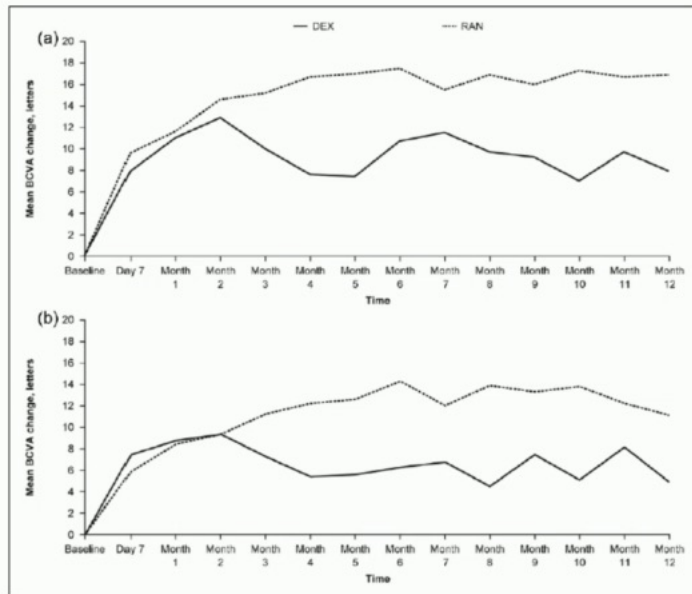
- Retrospective monocentric study
- 139 eyes of 139 patients
- BRVO with Rx naive macular edema
 - 69 eyes treated with bevacizumab (1 then PRN)
 - 70 eyes treated with DEX-i
- Higher N of HRF in the outer retina of BRVO eyes with ME ≥ 3 months
- Better BCVA gains with DEXi in eyes with ME ≥ 3 months: +17 vs. +7.5 letters ($p=0.017$)
 - Better HRF resolution with DEXi ($p<0.001$)



Randomized trial : The COMO study

COMO

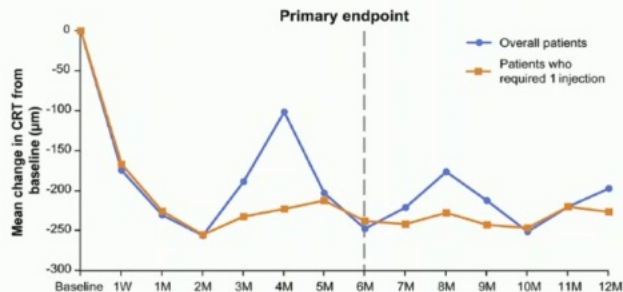
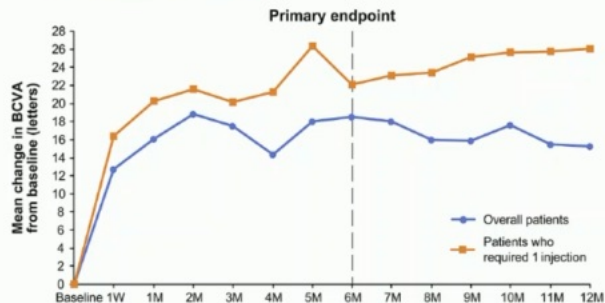
- 12-month, multicenter, randomized, openlabel trial
- Comparing
 - Ranibizumab (monthly through M5 then PRN)
 - DEXi at D0, M5 and M11
- BRVO related macular edema < 3 months
- A 5 month interval is not the best option



Prospective non-randomized trial: The COBALT study

COBALT

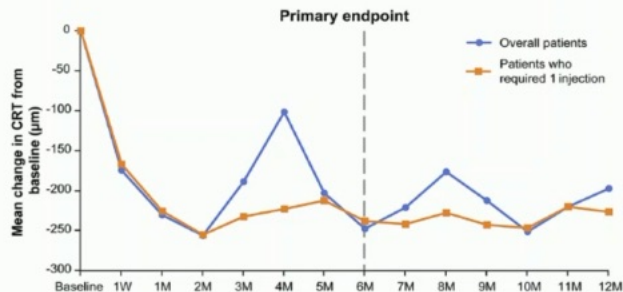
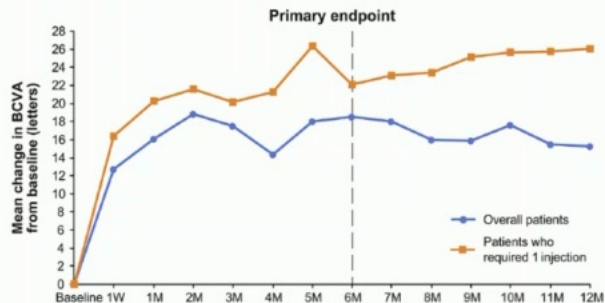
- Prospective, non comparative trial with 1 year of follow-up
- 71 eyes of 70 patients, treatment naive BRVO and ME<3months
- Reinjections possible every 4 months
- BCVA gains: 18.6 letters at 6 months ($p<0.0001$)



Prospective non-randomized trial: The COBALT study

COBALT

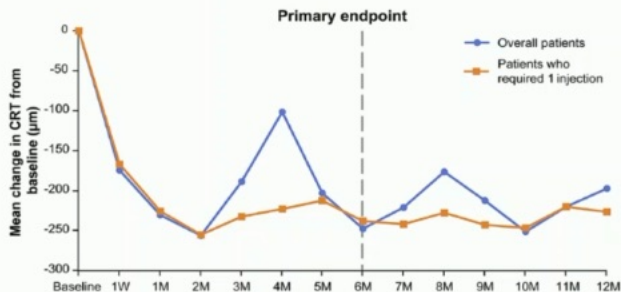
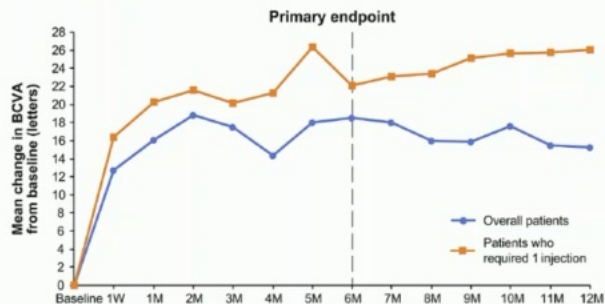
- Prospective, non comparative trial with 1 year of follow-up
- 71 eyes of 70 patients, treatment naive BRVO and ME<3months
- Reinjections possible every 4 months
- BCVA gains: 18.6 letters at 6 months ($p<0.0001$)
- ≥ 15 letters in 65% of patients at 6 months versus 22% in the GENEVA study



Prospective non-randomized trial: The COBALT study

COBALT

- Prospective, non comparative trial with 1 year of follow-up
- 71 eyes of 70 patients, treatment naive BRVO and ME<3months
- Reinjections possible every 4 months
- BCVA gains: 18.6 letters at 6 months ($p < 0.0001$)
- ≥ 15 letters in 65% of patients at 6 months versus 22% in the GENEVA study
- CMT reduction: -246.8 microns at 6 months ($p < 0.0001$)
- 70% of the maximal response starting D7
- N of IVI during the follow-up:
 - 1 injection in 32% of patients
 - 2 in 18% of patients
 - 3 in 49% of patients
- IOP increase: 35%, medical management only



Conclusion

- Dexamethasone implant is a good option to treat ME in RVO patients
- Early Rx provides better outcomes
- Injection intervals <4 months should be considered

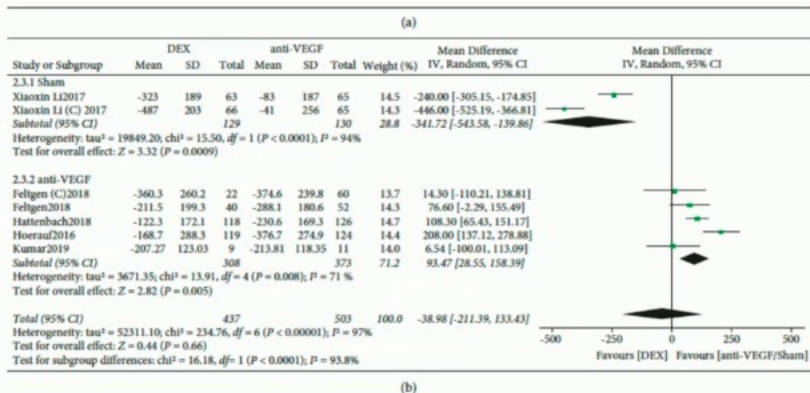


FIGURE 4: (a) Forest plot of BCVA for RVO-ME. (b) Forest plot of CRT for RVO-ME.



Indications to Perform Laser in RVO: Randomized Trials and Real-Life Data

Maurizio Battaglia Parodi, MD, FEBO

Department of Ophthalmology, IRCCS Ospedale San Raffaele,
Vita-Salute San Raffaele University, Milan, Italy

**Laser
is
not
dead !**

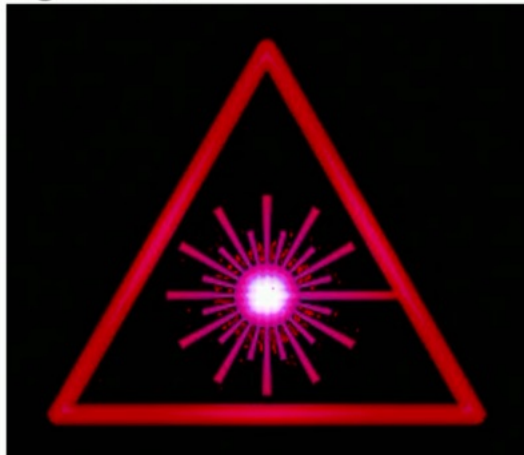


Laser Treatment for RVO

- Intravitreal approach revolutionized RVO management
 - Positive effects on ME
 - No effects on capillary non-perfusion
 - Delay of ocular NV development
- PRP/Peripheral scatter photocoagulation still useful

Laser Treatment for RVO

- Toward sequelae (ME & NV)
 - Panretinal/peripheral scatter photocoagulation
 - Grid laser treatment
- Toward RVO
 - Chorio-retinal venous anastomosis



Laser Treatment for RVO Complications

CRVO

- PRP
 - **Ischemic CRVO with NV YES**
 - Ischemic CRVO without NV Usually NO
- Macular Grid Laser
 - No indication
 - IV approach superior

BRVO

- Scatter Laser
 - **Ischemic BRVO with NV YES**
 - Ischemic BRVO without NV Usually NO
- Macular Grid Laser
 - Better than natural history
 - IV approach superior
 - Combined treatment ?
 - IV + Grid  Controversial outcomes

PRP for CRVO

- CVOS Group
 - PRP recommended in ischemic CRVO characterized by:
 - 2 Clock-Hours Iris NV or
 - Any Angle NV
- **PRP not indicated for simple ischemic CRVO**
- Challenging the identification of:
 - Ischemic CRVO in general
 - Ischemic CRVO which are more prone to develop ocular NV

CRVO Study Group Results

- Comparison between Early PRP vs Late PRP
- Early PRP performed before development of 2 Clock-Hours Iris NV or Any Angle NV

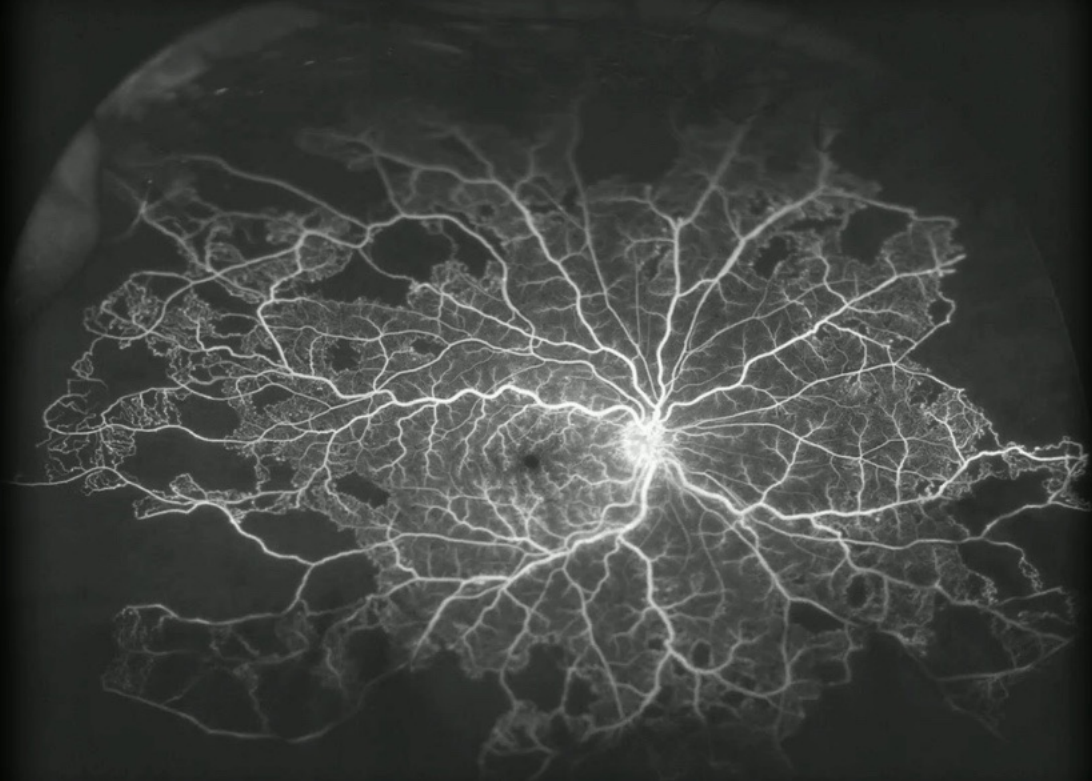
	Early PRP	Delayed PRP	
TC-INV, ANV or both	18/90 (20%)	32/91 (35%)	No Statistically Significant
NVD, NVE or both	11/90 (12%)	16/91 (18%)	No Statistically Significant
NV Glaucoma	5/90 (5.5%)	5/91 (5.5%)	No Statistically Significant

CRVO Study Group Results

- Comparison between Early PRP vs Late PRP
- Early PRP performed before development of 2 clock hours Iris NV or any Angle NV

	Early PRP	Delayed PRP	
TC-INV, ANV or both	18/90 (20%)	32/91 (35%)	No Statistically Significant
NVD, NVE or both	11/90 (12%)	16/91 (18%)	No Statistically Significant
NV Glaucoma	5/90 (5.5%)	5/91 (5.5%)	No Statistically Significant

- **No indication to Early PRP**
- **PRP does not completely prevent NV Glaucoma**



PRP in CRVO

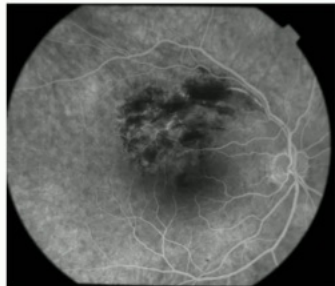
- Ischemic CRVO with evidence of 2 Clock-Hours Iris NV or Any angle NV
- **How to identify and monitor CRVO ?**
 - Identification of capillary non-perfusion not always easy
 - Combined information from relative afferent pupillary defect and ERG to differentiate 97% of ischemic CRVO cases
 - FA not always reliable
 - Classic definition of > 10 disc areas
 - Ultra Wide-Field FA unveiled extension of capillary non-perfusion
 - Unclear significance of capillary non-perfusion in the periphery
 - More importance to posterior pole
 - **Ischemic index >45, total non-perfusion area >75 DA, posterior pole non-perfusion >10 DA associated with higher NV risk**

Peripheral Scatter Photocoagulation for BRVO

- BRVO Study
 - Peripheral photocoagulation recommended when detected in ischemic BRVO (> 5 DD) characterized by
 - Retinal or optic disc NV
- **Peripheral photocoagulation not indicated for simple ischemic BRVO**
 - Visual field amputation
 - Limited NV rate development

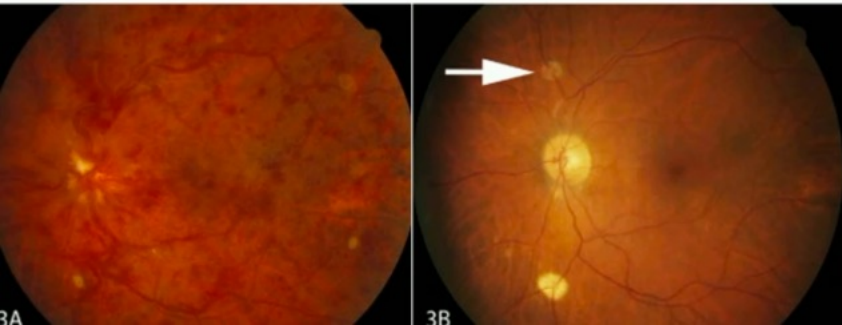
Macular Grid Laser for ME in BRVO

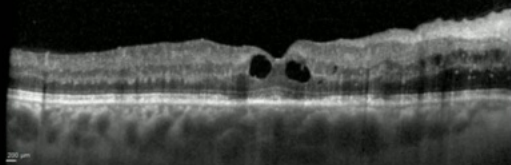
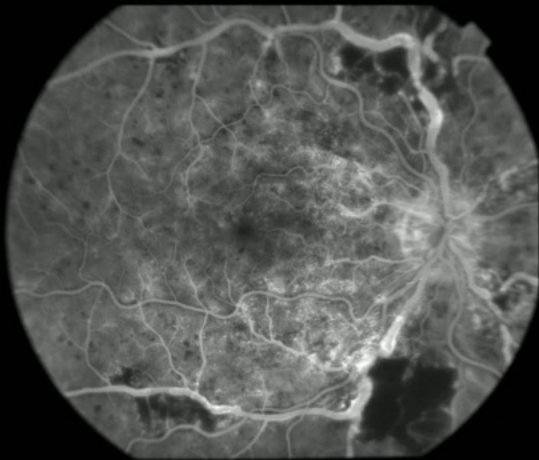
- RCT with grid tx vs natural history
 - Mean VA improvement of 1.3 lines
 - 2-line VA improvement in 65% of cases
 - Grid Group 65% vs non-T Group 37%
- **Grid laser photocoagulation leads to marginal VA improvement**
 - Better than natural history
 - IV approach superior with VA increase
 - Macular grid laser has similar effects with respect to natural history in Macular BRVO

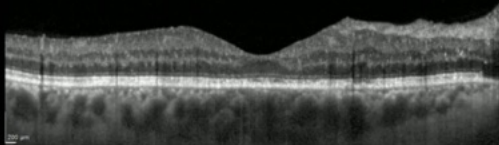


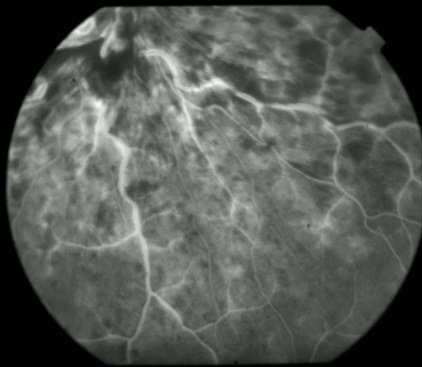
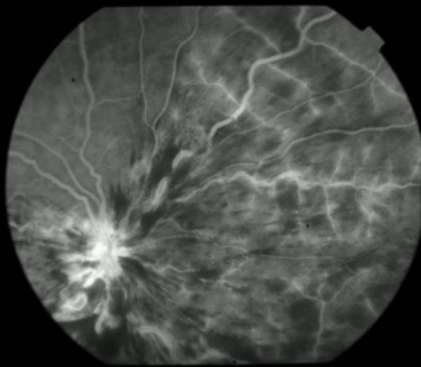
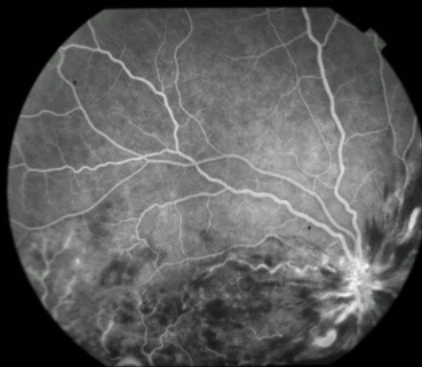
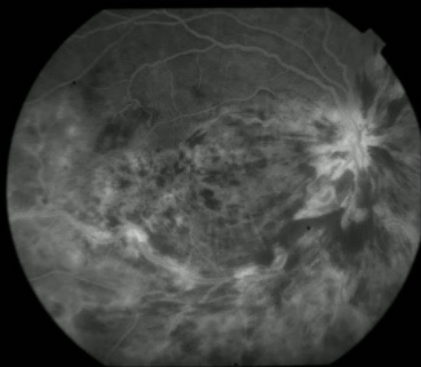
Chorio-Retinal Venous Anastomosis

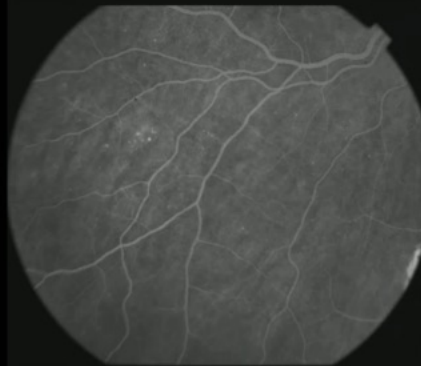
- Proposed by McAllister
- High-power laser burst to break BM and overlying vein
- Laser-induced communication between retinal vein and choroid to favour the venous outflow











Central Retinal Vein Bypass Study

- 113 eyes in RCT
- 18 months follow-up
- **Successful CRA in 76.4% of treatment arm**
- BCVA improvement
- Less progression to ischemia (4.9% vs 20.8%, $p = 0.03$)
 - Complications:
 - CNV (18%)
 - Vitrectomy (9%) for macular traction or vitreous hemorrhage

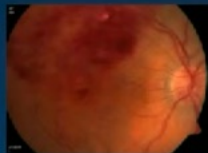
Conclusions

- Laser photocoagulation destructive treatment
- Useful to control ocular NV
- Awaiting new beneficial approaches

Update on BRVO and CRVO

Anat Loewenstein, MD

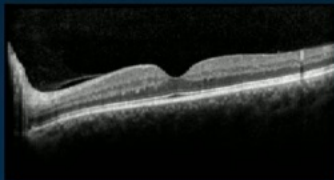
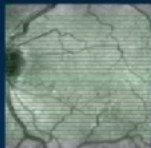
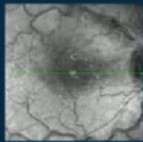
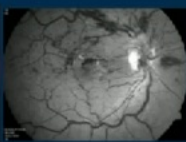
Professor & Director, Dept Ophthalmology, Tel Aviv Medical Center
Incumbent, Sidney A. Fox Chair in Ophthalmology
Vice Dean, Sackler Faculty of Medicine, Tel Aviv University
Israel



AB 52 years old gentleman

Decrease in VA in the right eye for the last month

VA 6/12 RE, 6/8 LE





Bilateral simultaneous Retinal Vein Occlusion in a young previously healthy man

CBC – 238,000 WBC !!!!!!!

HB – 13.9 Platelets – 280K

ESR – 2

PCR – BCR-ABL P210

Bone Marrow Aspiration

Chronic Myelocytic Leukemia confirmed

RVO - Risk Factors

Ocular diseases

Systemic vascular disorders

Inflammatory/
autoimmune diseases

Hematological abnormalities

brovacizumab



Glaucoma
Increased IOP

Hypertension
ASCVD
Diabetes

SLE

Hyperlipidemia
Hyperviscosity
syndromes
Coagulation cascade
abnormalities



RVO - Risk Factors

Cardiovascular risk factors are the most common risk factors for RVO

- Hypertension in ≥ 50 yrs is predominant risk factor**
- Hyperlipidaemia is a common risk factor**
- Diabetes is associated with RVO, but perhaps because both are associated with cardiovascular risk factors**



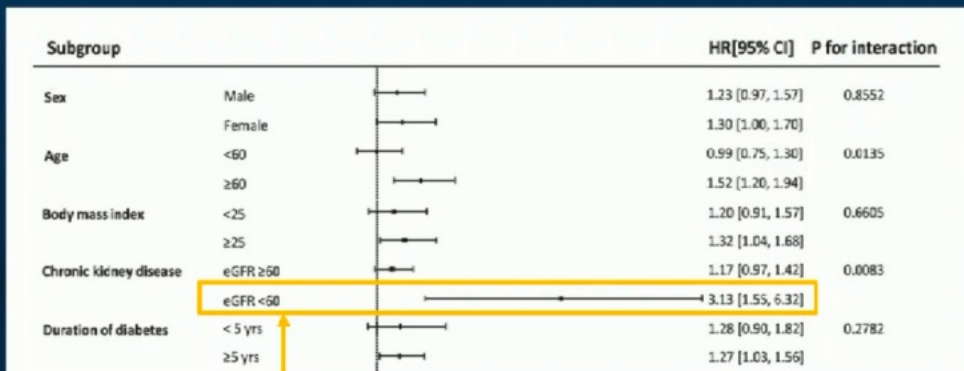
Reserving systemic investigation to those patients who

- Lack usual risk factors**
- Present with simultaneous bilateral disease**

- Extensive history**
- Focus on bleeding or clotting tendency**
- Family history looking for thrombophilia**

- Results of the history should guide the investigation rather than doing extensive workout to all patients**

RVO - Risk Factors



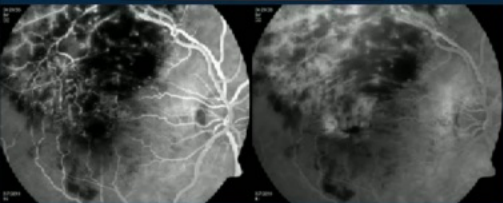
SGLT2 Inhibitors should be used carefully among chronic renal patients

RVO - Clinical Examination

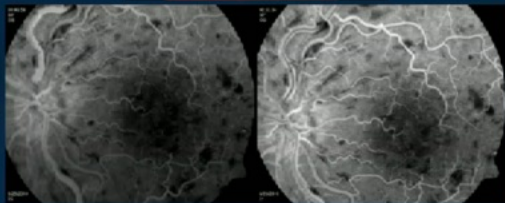
BRVO



CRVO



FA

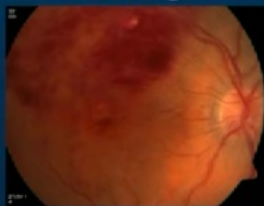


OCT

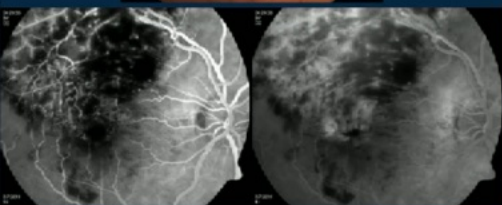


RVO - Clinical Examination

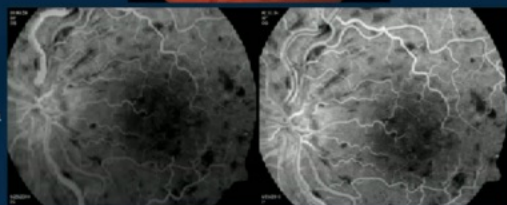
BRVO



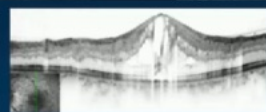
CRVO



FA

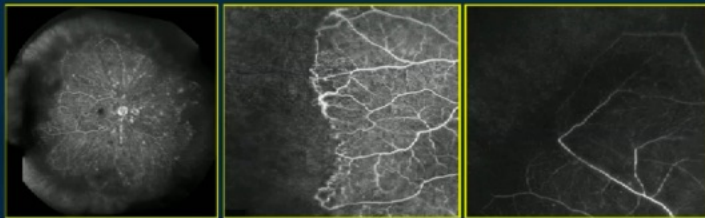


OCT



Wide field angiography

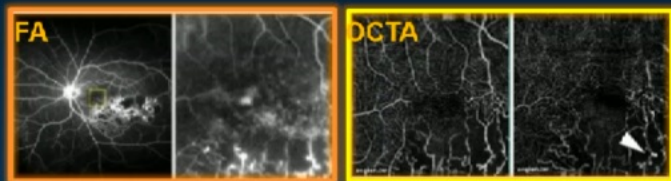
- Vascular nonperfusion in the periphery



- No correlation between nonperfused areas and
 - Visual acuity outcome
 - Number of injections

OCT Angiography

- ✓ High resolution – clear images of non-perfused areas
- ✓ No obstruction by hyperpermeable vessels (no dye)
- ✓ Visualization of microvascular abnormalities & collaterals
- ✓ Differential layer analysis of microaneurysms and collateral vessels
- ✓ Minimal impairment by retinal hemorrhages



Was not shown to change

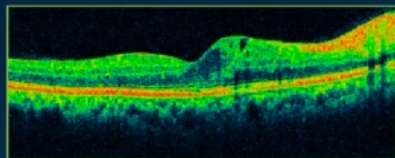
- Visual acuity outcome
- Number of injections

56 y old lady, Hypertension

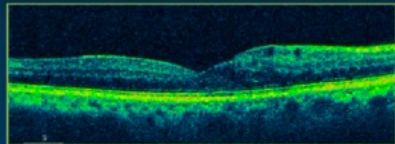
6 week decrease in visual acuity



s/p 2 Ranibizumab



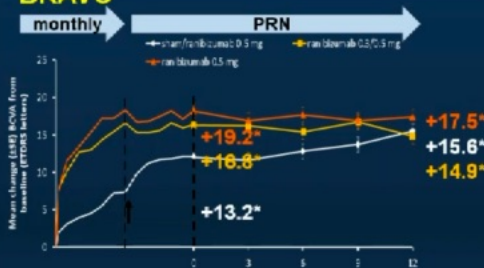
Last follow up
s/p 4 injections
6/9



RVO trials

- Control group was slow to achieve improvement in VA and did not achieve same level

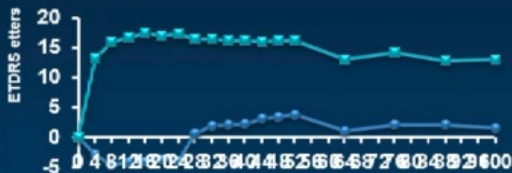
BRAVO



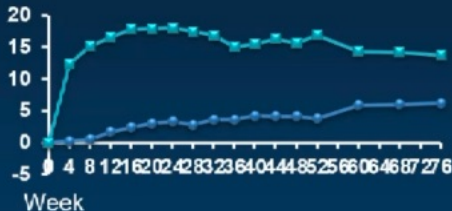
CRUISE



COPERNICUS



GALILEO



CENTERA Study

Phase 4 study evaluating aflibercept in T&E regimen for macular edema, secondary to CRVO, for 3 months

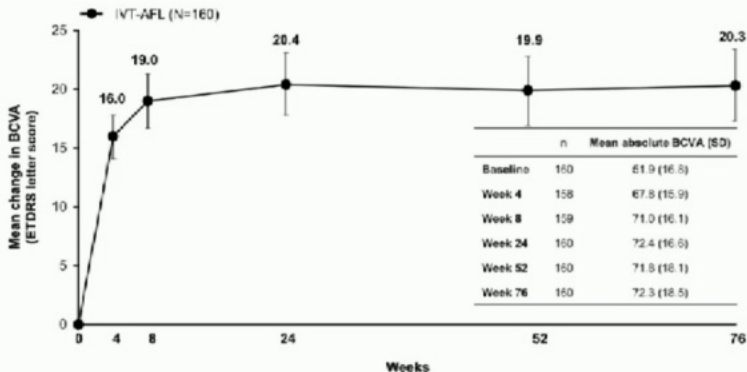


FIGURE 2. Mean change in BCVA from baseline to week 76. Full analysis set; last observation carried forward. Error bars are 95% confidence intervals. BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; IVT-AF = intravitreal aflibercept; SD = standard deviation.

CENTERA Study

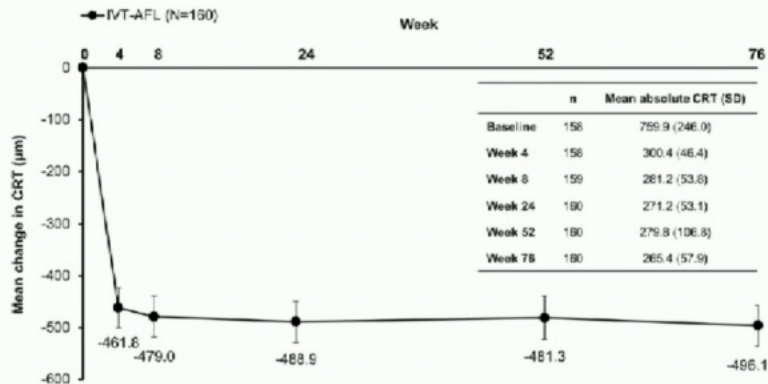


FIGURE 3. Mean change in CRT from baseline to week 76. Full analysis set; last observation carried forward. Error bars are 95% confidence intervals. Change at week 4, n = 156; n = 157 at week 8; and n = 158 at weeks 24, 52, and 72. CRT = central retinal thickness; IVT-AFL = intravitreal aflibercept; SD = standard deviation.

SCORE2

Baseline Factor ^a	Resolution of Macular Edema			CST < 300 μ m			Change From Baseline		
	No. of Eyes With Nonimproving Data	No. (%) Resolved	Unadjusted P Value	No. of Eyes With Nonimproving Data	No. (%) With CST < 300 μ m	Unadjusted P Value	No.	Mean (SD)	Unadjusted P Value
Total	341	141 (41.3)	NA	335	281 (83.9)	NA	328	-495.5 (245.2)	NA
Treatment arm									
Aflibercept	169	92 (54.4)	NA	164	154 (93.9)	NA	160	-425.1 (230.5)	NA
Bevacizumab	172	49 (28.5)	<.001	171	127 (74.3)	<.001	168	-386.8 (257.7)	.16
Ethnicity									
Non-Hispanic	308	127 (41.2)	NA	302	254 (84.1)	NA	297	-396.9 (246.5)	NA
Hispanic	33	14 (42.4)	.89	33	27 (81.8)	.73	31	-487.7 (219.3)	.05
Smoking status									
Never smoker	187	83 (44.4)	NA	182	156 (85.7)	NA	180	-445.0 (264.4)	NA
Prior smoker	120	48 (40.0)	.45	120	96 (80.0)	.19	116	-350.1 (213.3)	.001
Current smoker	34	19 (29.4)	.11	33	29 (87.9)	.74	32	-384.0 (201.6)	.19
e-ETDRS visual acuity letter score									
59-73 (20/40 to 20/63)	128	51 (39.8)	NA	127	111 (87.4)	NA	123	-302.1 (196.5)	NA
49-58 (20/80 to 20/100)	78	43 (55.1)	NA	78	64 (82.1)	NA	78	-387.1 (182.5)	NA
19-48 (20/125 to 20/400)	135	47 (34.8)	NA	130	106 (81.5)	NA	127	-515.9 (274.0)	NA
Continuous (pre-2-week increase in score)	NA	NA	NA	NA	NA	.89	NA	NA	<.001
Time between diagnosis of macular edema and randomization, mo									
<2	213	105 (49.4)	NA	213	178 (83.6)	NA	210	-432.4 (251.4)	NA
≥ 2	128	38 (29.7)	NA	122	103 (84.4)	NA	118	-357.6 (226.9)	NA
Continuous (pre-2 mo increase)	NA	NA	.002	NA	NA	.88	NA	NA	.02
Lens status									
Normal lens	256	114 (44.5)	NA	251	212 (84.5)	NA	247	-421.8 (241.8)	NA
Prior lens extraction	85	27 (31.8)	.04	84	69 (82.1)	.62	81	-355.7 (250.0)	.04
Prior anti-VEGF treatment									
No	228	114 (50.0)	NA	227	192 (84.6)	NA	222	-421.2 (245.8)	NA
Yes	113	27 (23.9)	<.001	108	89 (82.4)	.61	106	-372.7 (241.8)	.09
Prior steroid treatment									
No	317	135 (42.6)	NA	312	261 (83.7)	NA	305	-414.0 (248.0)	NA
Yes	24	6 (25.0)	.10	23	20 (87.0)	.68	23	-293.1 (170.5)	.02
Type of occlusion									
CRVO	285	124 (43.5)	NA	279	235 (84.2)	NA	274	-418.4 (245.1)	NA
BRVO	56	17 (30.4)	.07	56	46 (82.1)	.70	54	-339.8 (237.1)	.03



SCORE2

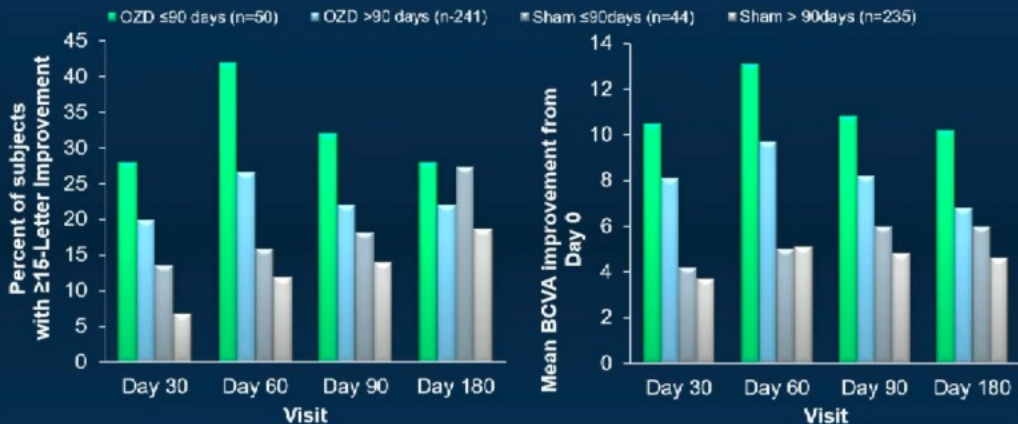
Baseline Factor ^a	Resolution of Macular Edema			CST < 300 µm			Change From Baseline		
	No. of Eyes With Nonmissing Data	No. (%) Resolved	Unadjusted P Value	No. of Eyes With Nonmissing Data	No. (%) With CST < 300 µm	Unadjusted P Value	No.	Mean (SD)	Unadjusted P Value
Total	341	141 (41.3)	NA	335	281 (83.9)	NA	328	-405.5 (245.2)	NA
Treatment arm									
Aflibercept	169	92 (54.4)	NA	164	154 (93.9)	NA	160	-425.1 (230.5)	NA
Bevacizumab	172	49 (28.5)	<.001	171	127 (74.3)	<.001	168	-385.8 (257.7)	.16
Ethnicity									
Non-Hispanic	308	127 (41.2)	NA	302	254 (84.1)	NA	297	-396.9 (246.5)	NA
Hispanic	33	14 (42.4)	.89	33	27 (81.8)	.73	31	-487.7 (219.3)	.05
Smoking status									
Never smoker	187	83 (44.4)	NA	182	156 (85.7)	NA	180	-445.0 (264.4)	NA
Prior smoker	120	48 (40.0)	.45	120	96 (80.0)	.19	116	-350.1 (213.3)	.001
Current smoker	34	19 (29.4)	.11	33	29 (87.9)	.74	32	-384.0 (201.6)	.19
e-ETDRS Visual acuity letter score									
≤20/70 (20/40 to 20/60)	128	51 (39.8)	NA	127	111 (87.4)	NA	123	-300.1 (196.5)	NA

Time between diagnosis of macular edema and randomization, mo

<2	213	103 (48.4)	NA	213	178 (83.6)	NA	210	-432.4 (251.4)	NA
≥2	128	38 (26.7)	NA	122	103 (84.4)	NA	118	-357.6 (226.9)	NA
Continuous (per 1-mo increase)	NA	NA	.003	NA		.48	NA	NA	.03

(increase)									
Lens status									
Normal lens	256	114 (44.5)	NA	251	212 (84.5)	NA	247	-421.8 (241.8)	NA
Prior lens extraction	85	27 (31.8)	.04	84	69 (82.1)	.62	81	-355.7 (250.0)	.04
Prior anti-VEGF treatment									
No	228	114 (50.0)	NA	227	192 (84.6)	NA	222	-421.2 (245.8)	NA
Yes	113	27 (23.9)	<.001	108	89 (82.4)	.61	106	-372.7 (241.8)	.09
Prior steroid treatment									
No	317	135 (42.6)	NA	312	261 (83.7)	NA	305	-414.0 (248.0)	NA
Yes	24	5 (25.0)	.10	23	20 (87.0)	.68	23	-293.1 (170.5)	.02
Type of occlusion									
CRVO	285	124 (43.5)	NA	279	235 (84.2)	NA	274	-418.4 (245.1)	NA
BRVO	56	17 (30.4)	.07	56	46 (82.1)	.70	54	-339.8 (237.1)	.03

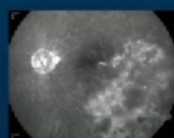
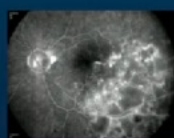
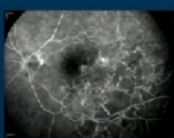
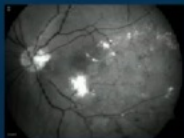
Patients treated by Ozurdex with shorter edema duration had better final outcome



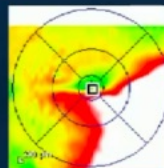
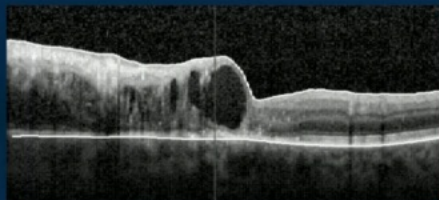
- A post hoc analysis showed that eyes treated within 90 d since onset of ME were more likely to improve than eyes in which treatment was instituted after this time point

KI, 66 y old

sp 11 Bevacizumab, 6 ranibizumab, ozurdex

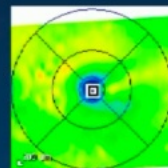
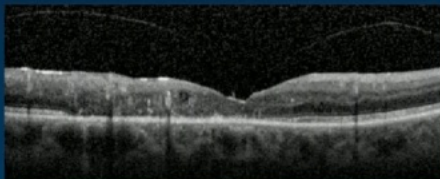


39 m f/u
VA 1/24



Scatter laser

44 m f/u





PRP to peripheral areas of NP for VA & injection frequency

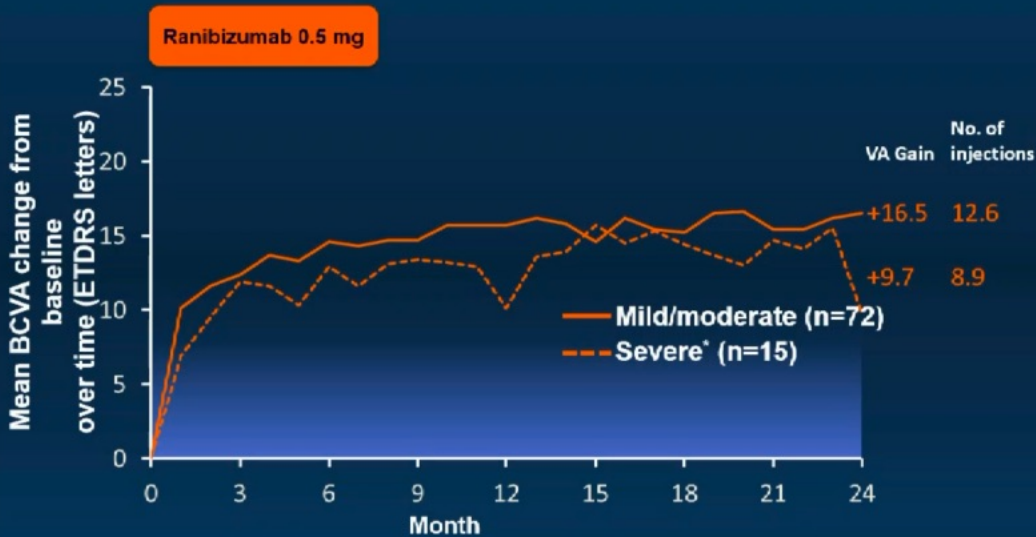
Prospective study of 10 pts with CRVO

- **Purpose: To investigate effect of PRP on VA & injection frequency of ranibizumab**
- **Pts were imaged with wide-field angiography before & after laser**
- **Injection frequency did not change between the 6-mo lead-in period or in the 6-mo follow up period**
- **VA also remained unchanged**

Conclusion

- **Laser to peripheral areas of NP did not result in either decreased injection frequency or improved VA**

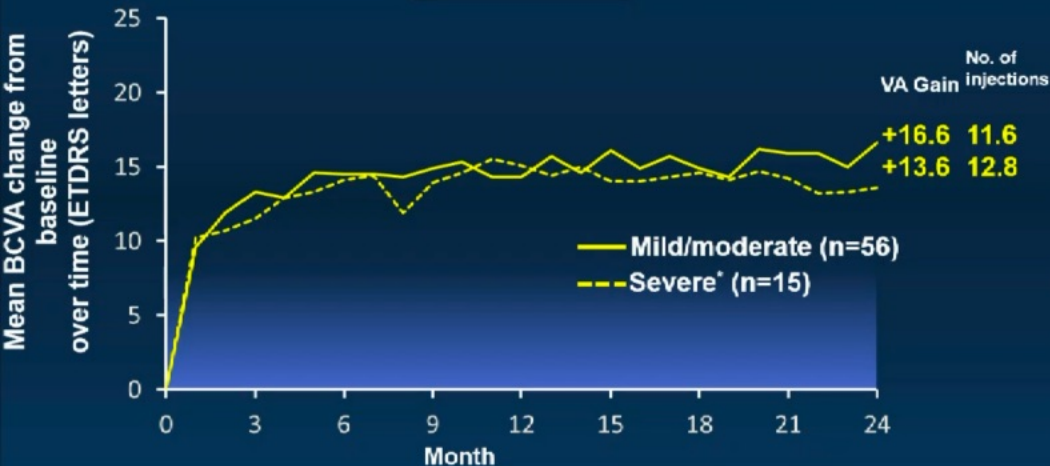
BRIGHTER 24m: ranibizumab mono therapy provided BCVA gains irrespective of severity of ischemia





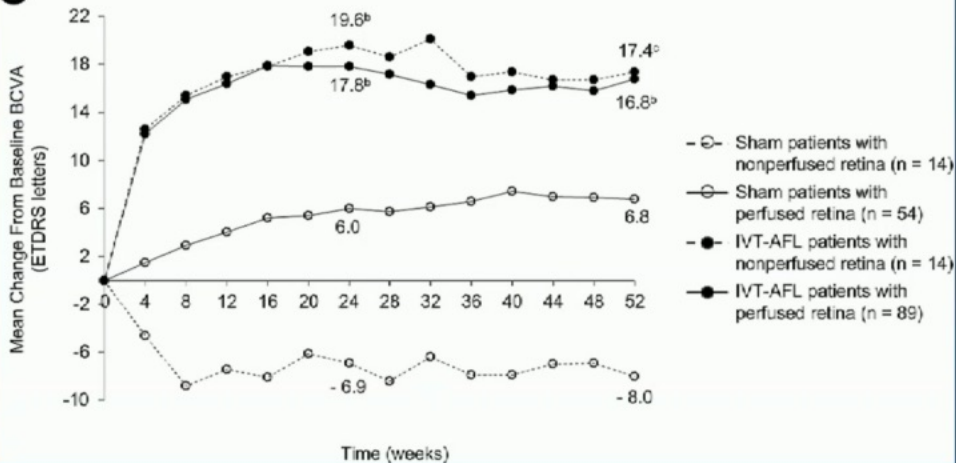
BRIGHTER 24m: ranibizumab + laser therapy provided BCVA gains irrespective of severity of ischemia

Ranibizumab 0.5 mg +
adjunctive laser†



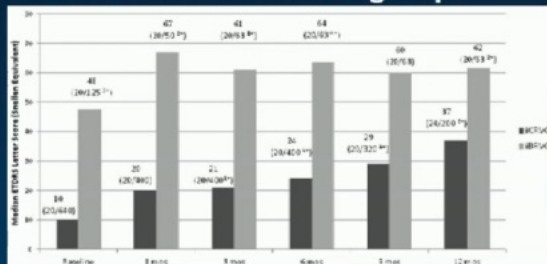
GALILEO Study

C



Ozurdex was beneficial for ischemic BRVO and CRVO

- Prospective, open-label, noncomparative, nonrandomized interventional case series, with a follow-up of 12 months
- 15 patients with central ischemic RVO and 14 patients with branch ischemic RVO were injected with 700 µg dexamethasone implant at baseline and then PRN starting from the 4th month
- A improved from 10 to 37 letters at 12 months in the CRVO group and from 48 to 62 in the BRVO group

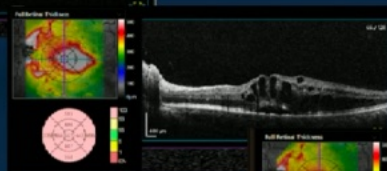


**Mean No. of injection
2.8 in CRVO, 2 in BRVO**

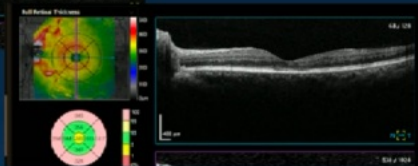
70 y.o female, HTN
Decreased vision LE – BCVA 6/15
LE perfused CRVO



s/p Bevacizumab *3
BCVA 6/30



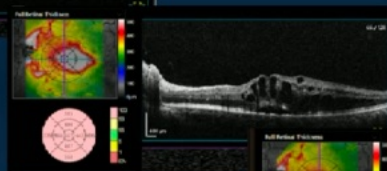
s/p Aflibercept *3
BCVA 6/7.5



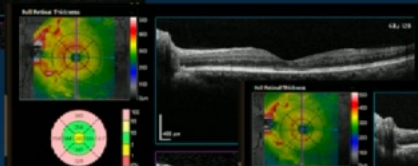
70 y.o female, HTN
Decreased vision LE – BCVA 6/15
LE perfused CRVO



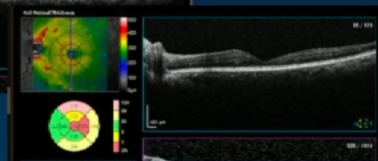
s/p Bevacizumab *3
BCVA 6/30



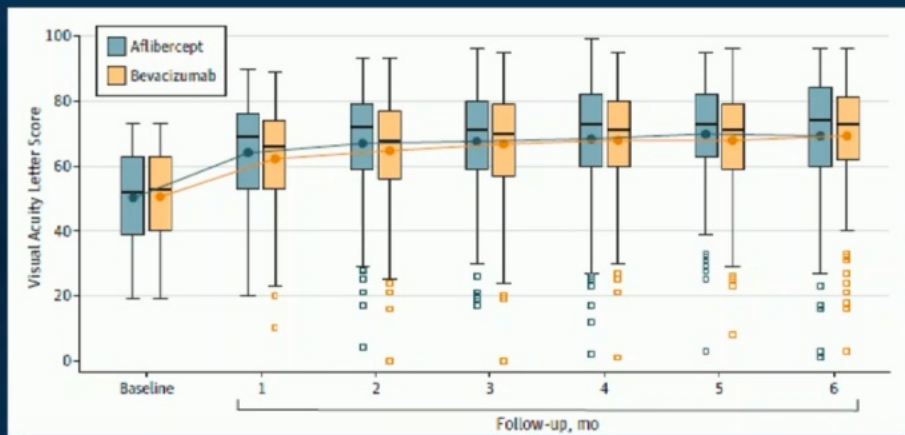
s/p Aflibercept *3
BCVA 6/7.5



4 y later (TER)
BCVA 6/8.5



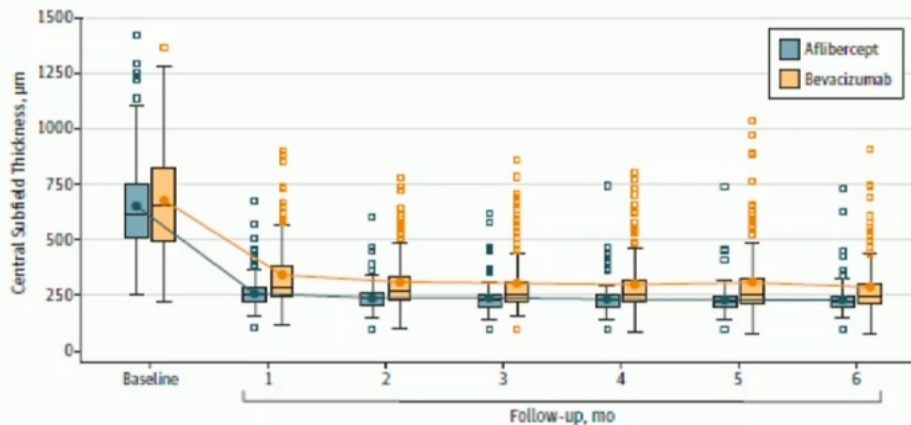
SCORE2: Visual Acuity Letter Score at Baseline and Monthly Through Month 6



At month 6, bevacizumab was non-inferior to aflibercept based on a VALS margin of 5 (P for non-inferiority = 0.001)

SCORE-2 TRIAL

Figure 3. Spectral-Domain Optical Coherence Tomography Central Subfield Thickness at Baseline and Monthly Through Month 6



Eyes, No.

Aflibercept	173	167	169	167	164	161	164
Bevacizumab	178	171	176	174	169	166	171

LEAVO: study design

LEAVO (N=463)

Multicenter, double-masked, randomized, controlled, non-inferiority Phase III trial comparing clinical and cost effectiveness of intravitreal therapy with ranibizumab, aflibercept, and bevacizumab for macular edema due to CRVO

Patients randomized 1:1:1

Ranibizumab 0.5 mg (n=155)

Aflibercept 2 mg (n=154)

Bevacizumab 1.25 mg (n=154)

4 initial monthly injections, followed by PRN therapy every 4–8 weeks if prespecified retreatment criteria were met

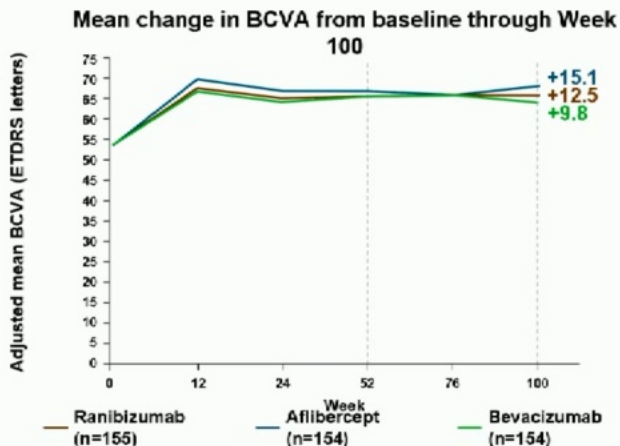
Primary endpoint:
Change in BCVA from baseline to Week 100

Week 52: Interim analysis

Week 100: Primary endpoint

Selected secondary endpoints:
Mean CST and macular volume at Weeks 52 and 100; quality of life, and resource utilization

LEAVO: Visual outcomes from baseline through Week 100 (primary endpoint)



LEAVO: Non-inferiority (adjusted difference – primary endpoint)

Intergroup comparisons	Week 52	Week 100 (primary endpoint)
Aflibercept vs. ranibizumab	Non-inferior	Non-inferior
Bevacizumab vs. aflibercept	Not non-inferior	Not non-inferior

Intergroup comparisons	Non-inferiority test Week 52	Week 100 (primary endpoint)
Aflibercept vs. ranibizumab	Passed	Passed
Bevacizumab vs. aflibercept*	Failed	Failed
Bevacizumab vs. ranibizumab	Passed	Failed

LEAVO: Non-inferiority (adjusted difference – primary endpoint)

Intergroup comparisons	Week 52	Week 100 (primary endpoint)
Aflibercept vs. ranibizumab	Non-inferior	Non-inferior
Bevacizumab vs. aflibercept	Not non-inferior	Not non-inferior

Intergroup comparisons	Non-inferiority test Week 52	Week 100 (primary endpoint)
Aflibercept vs. ranibizumab	Passed	Passed
Bevacizumab vs. aflibercept*	Failed	Failed
Bevacizumab vs. ranibizumab	Passed	Failed

LEAVO: Post Hoc Analysis

eTable 4. Comparing differences in CST resolution pattern between drugs

	Aflibercept, % (n/N)	Bevacizumab, % (n/N)	Ranibizumab, % (n/N)	Difference, %; (95% CI); P value Ranibizumab vs Aflibercept	Difference, %; (95% CI); P value Ranibizumab vs Becavizumab	Difference, %; (95% CI); P value Becavizumab vs Aflibercept
Dry by 100 weeks	42.5% (57/134)	20.0% (28/140)	23.4% (32/137)	19.2% (6.2,30.1) P<.001	-3.4% (-13.1,8.3) P=.50	22.5% (11.9,33.2) P<.001
Recurrent by 100 weeks	52.2% (70/134)	61.4% (86/140)	68.6% (94/137)	-16.4% (-27.9,-4.9) P=.006	-7.2% (-18.4,4.0) P=.21	-9.2% (-20.9,2.5) P=.12
Wet by 100 weeks	5.2% (7/134)	18.6% (26/140)	8.0% (11/137)	-2.8% (-8.7,3.1) P=.35	10.5% (2.7,18.4) P=.01	-13.3% (-20.8,-5.9) P<.001
Dry by 52 weeks	63.6% (75/140)	27.8% (40/144)	37.9% (53/140)	15.7% (4.1,27.2) P=.008	-10.1% (-20.9,0.8) P=.08	25.8% (14.8,36.8) P<.001
Recurrent by 52 weeks	40.0% (56/140)	48.6% (70/144)	46.3% (65/140)	-6.4% (-18.0,5.2) P=.28	2.2% (-9.4,13.8) P=.71	-6.6% (-20.1,2.9) P=.14
Wet by 52 weeks	6.4% (9/140)	23.6% (34/144)	15.7% (22/140)	-9.3% (-18.6,-2.0) P=.01	7.9% (-1.3,17.1) P=.09	-17.2% (-25.2,-9.1) P<.001

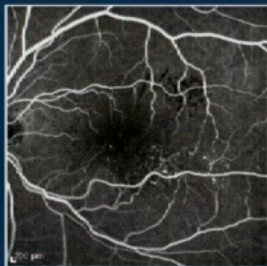
Macular Edema Status	Mean BCVA Gain
Persistent Dry	16.8
Recurrent	13.1
Wet	6.4

**Association
between ME
and BCVA**

TS, 77 y old lady

- Decreased vision for 3 w in left eye
- Past history: stroke 1 m prior

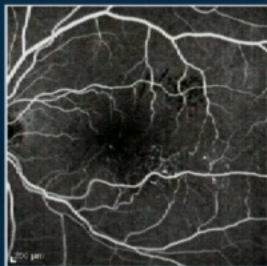
6/15



TS, 77 y old lady

- Decreased vision for 3 w in left eye
- Past history: stroke 1 m prior

6/15



Ozurdex

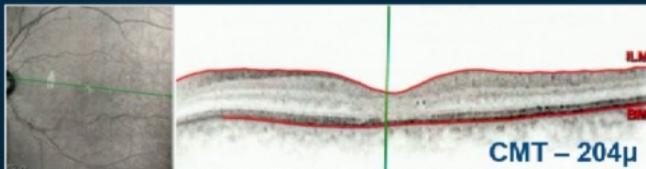


Prior to ODX
BCVA – 6/15
T – 12 mmHg



Ozurdex

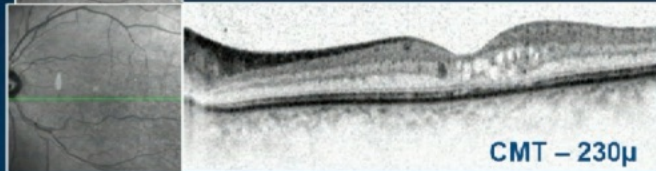
6 w post
ozurdex
BCVA – 6/15
T – 16 mmHg



20 w post
ozurdex
BCVA – 6/12
T – 12 mmHg



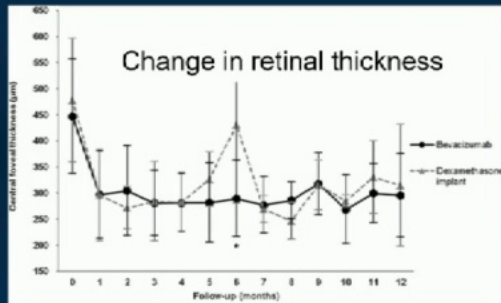
36 w post
ozurdex
BCVA – 6/15



Ozurdex vs. bevacizumab for BRVO

Retrospective study

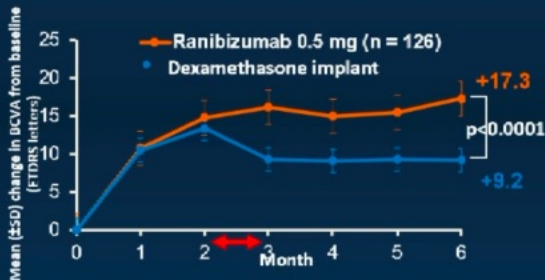
- 72 pts treated with either PRN bevacizumab or ozurdex (every 6 mo)



- No statistical differences between BCVA
- CRT deteriorated at 6 mo in DEX group, but was restored after treatment; no sig. differences at 12 mo

COMRADE-B (BRVO)

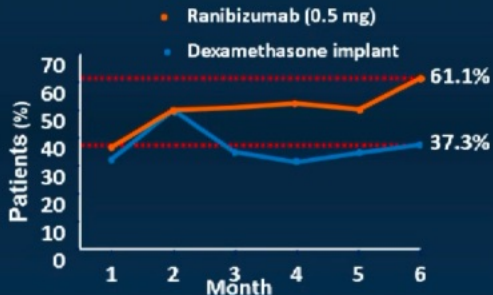
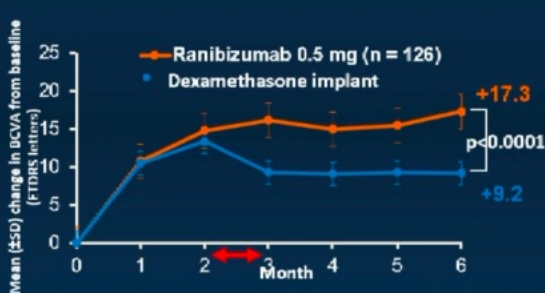
- Head-to-head trial comparing RBZ with dexamethasone in BRVO
- RBZ superior efficacy to dexamethasone implant over 6 months



Effect on BCVA with dexamethasone diminished at 3 months, suggesting patients may require repeat dosing with dexamethasone prior to Month 6

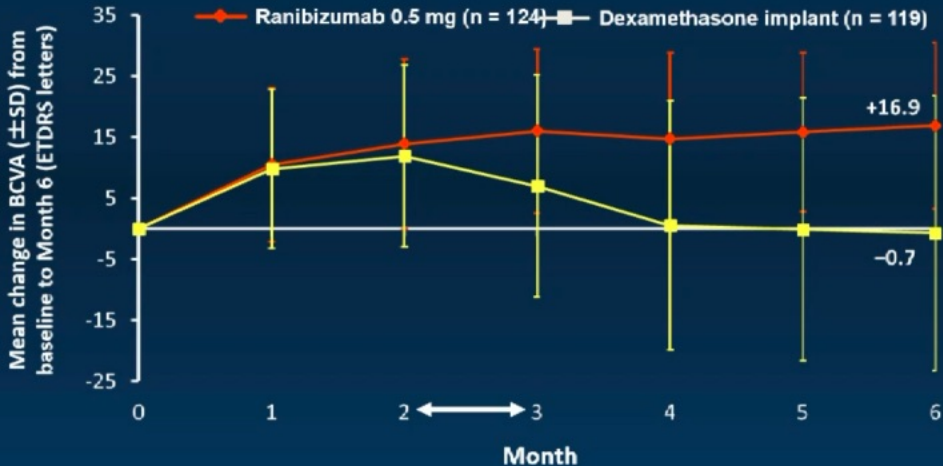
COMRADE-B (BRVO)

- Head-to-head trial comparing RBZ with dexamethasone in BRVO
- RBZ superior efficacy to dexamethasone implant over 6 months



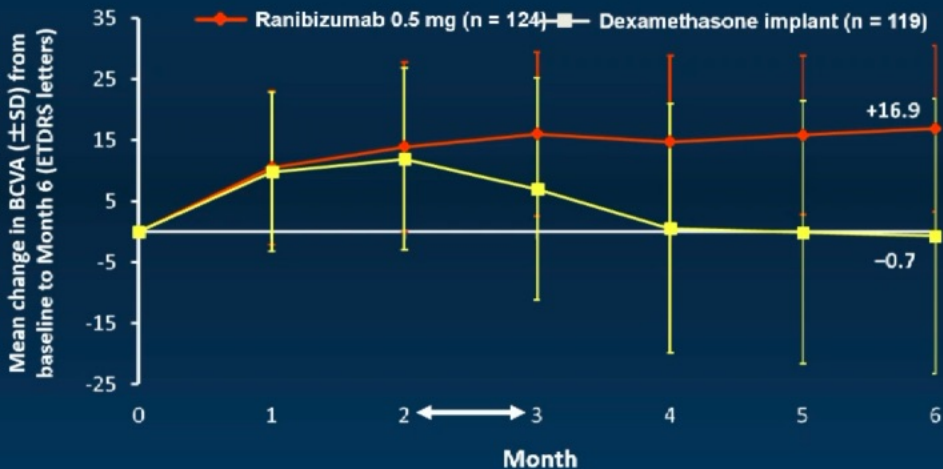
Effect on BCVA with dexamethasone diminished at 3 months, suggesting patients may require repeat dosing with dexamethasone prior to Month 6

COMRADE-C: efficacy of ranibizumab PRN at 6 months compared with single dexamethasone implant*



*Primary endpoint met: Mean change in BCVA from baseline to Month 1 through Month 6 was superior with ranibizumab compared with dexamethasone implant ($p < 0.0001$); Full analysis set, last observation carried forward.

COMRADE-C: efficacy of ranibizumab PRN at 6 months compared with single dexamethasone implant*



*Primary endpoint met: Mean change in BCVA from baseline to Month 1 through Month 6 was superior with ranibizumab compared with dexamethasone implant ($p < 0.0001$); Full analysis set, last observation carried forward.

Anti-VEGF Therapy - BRVO

IVR 0.5mg PRN	0.46 (0.026 to 0.85)	-	0.74 (0.055 to 1.0)	0.59 (0.025 to 1.0)	0.16 (0.025 to 0.95)	-	0.80 (0.011 to 1.6)
1.3 (0.13 to 1.9)	IVR 0.5mg monthly	-	1.0 (0.18 to 1.8)	1.3 (0.075 to 2.2)	0.34 (0.036 to 0.6)	-	0.22 (0.037 to 0.4)
1.1 (0.26 to 4.7)	0.83 (0.050 to 1.2)	IVR + Laser	-	-	-	-	-
-	-	-	IVA 2 mg monthly	0.81 (0.13 to 4.9)	4.7 (0.74 to 31)	-	0.14 (0.036 to 0.51)
-	-	-	-	IVB 1.25mg monthly	3.8 (0.29 to 51)	-	0.17 (0.019 to 1.6)
-	-	-	-	-	-	-	-
0.18 (0.065 to 1.0)	0.28 (0.045 to 1.7)	0.34 (0.044 to 2.7)	-	-	IVD 0.7mg	-	0.05 (0.18 to 2.5)
0.47 (0.10 to 2.0)	0.35 (0.022 to 5.2)	0.42 (0.095 to 1.9)	-	-	1.2 (0.16 to 9.7)	Laser	-
0.34 (0.057 to 2.2)	0.23 (0.058 to 1.1)	0.11 (0.032 to 0.32)	-	-	0.90 (0.32 to 2.7)	0.73 (0.075 to 7.9)	Placebo/Sham

Central retinal vein occlusion

Branch retinal vein occlusion

A meta-analysis compared ranibizumab, bevacizumab and aflibercept in BRVO/CRVO

The most effective treatments for BRVO were: monthly dosage of ranibizumab, PRN ranibizumab (after the initial 3 injections) and ranibizumab combined with laser

Anti-VEGF Therapy - CRVO

IVR 0.5mg 3PRN	0.45 (0.028 to 0.5)	-	0.74 (0.055 to 1.0)	0.59 (0.025 to 1.5)	0.16 (0.025 to 0.95)	-	0.10 (0.011 to 1.0)
1.3 (0.13 to 15)	IVR 0.5mg monthly	-	1.6 (0.18 to 15)	1.5 (0.075 to 22)	0.34 (0.036 to 3.2)	-	0.22 (0.037 to 1.4)
1.1 (0.26 to 4.7)	0.85 (0.050 to 12)	IVR + Laser	-	-	-	-	-
-	-	-	IVA 2mg monthly	0.81 (0.15 to 4.9)	4.7 (0.74 to 31)	-	0.14 (0.036 to 0.51)
-	-	-	-	IVB 1.25mg monthly	3.8 (0.25 to 51)	-	0.17 (0.019 to 1.6)
-	-	-	-	-	-	-	-
0.38 (0.085 to 1.5)	0.28 (0.045 to 1.7)	0.34 (0.044 to 2.7)	-	-	IVD 0.7mg	-	0.65 (0.18 to 2.5)
0.47 (0.10 to 2.0)	0.35 (0.02 to 5.2)	0.42 (0.098 to 1.9)	-	-	1.2 (0.15 to 9.7)	Laser	-
0.34 (0.057 to 2.2)	0.25 (0.058 to 1.1)	0.31 (0.032 to 3.2)	-	-	0.90 (0.32 to 2.7)	0.78 (0.075 to 7.9)	Placebo/Sham

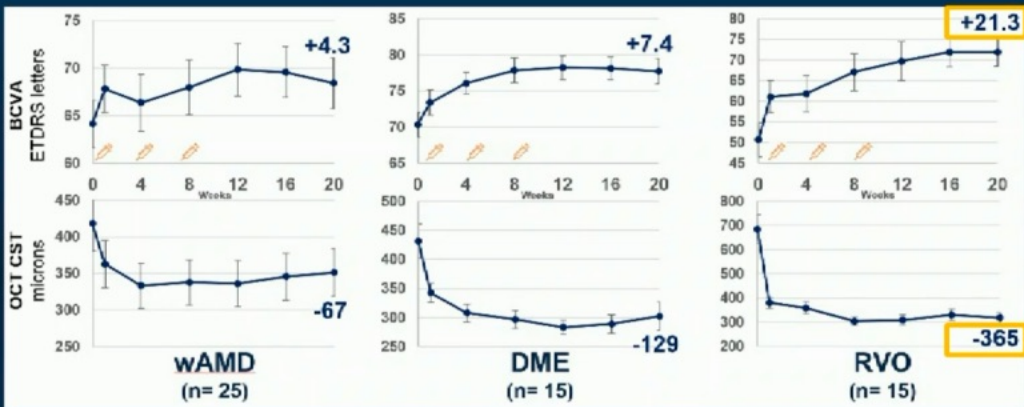
Central retinal vein occlusion

Branch retinal vein occlusion

A meta-analysis compared ranibizumab, bevacizumab and aflibercept in BRVO/CRVO

The most effective treatments for CRVO were: PRN ranibizumab, then aflibercept with monthly dosage and then bevacizumab with monthly dosage of 1.25mg

The Potential of Long Acting Anti VEGF For RVO: KSI-301



A Phase 1b clinical trial has demonstrated promising initial safety, efficacy and durability of KSI-301, a novel anti-VEGF antibody biopolymer conjugate in patients with wet AMD, DME/DR and RVO

109 patients enrolled. Patients received 3 initial monthly doses of either 2.5 mg or 5 mg of KSI-301 with additional treatment given according to disease-specific, protocol-specified retreatment criteria.

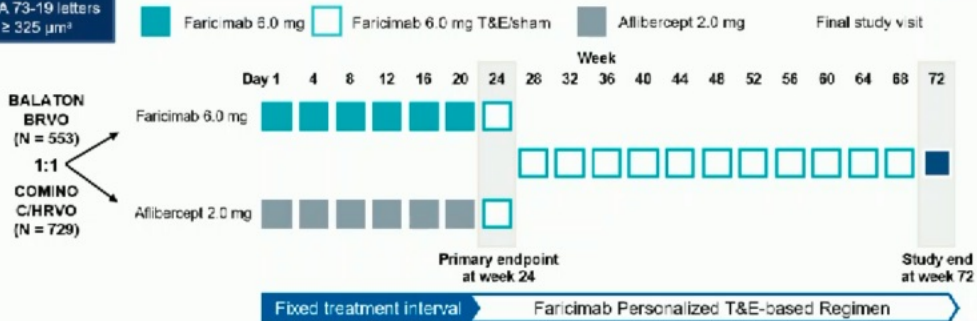
BALATON and COMINO

Phase 3, Randomized, Double-Masked, Multicenter Trials Designed to Evaluate the Efficacy and Safety of Faricimab vs Aflibercept

Key Inclusion criteria

- Age ≥ 18 years
- Treatment-naïve macular edema due to RVO
- BCVA 73-19 letters
- CST $\geq 325 \mu\text{m}^2$

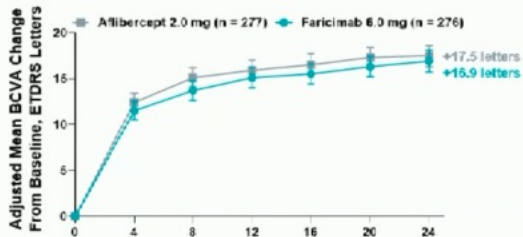
Primary endpoint: Change from baseline in BCVA[†] at week 24 (faricimab vs aflibercept)



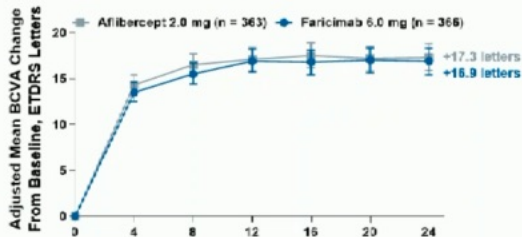
BALATON BRVO (N = 553)
1:1
COMINO C/HRVO (N = 729)

Faricimab Achieved Robust Vision Gains in Both Trials: Results Were Comparable Between Treatment Arms

BALATON



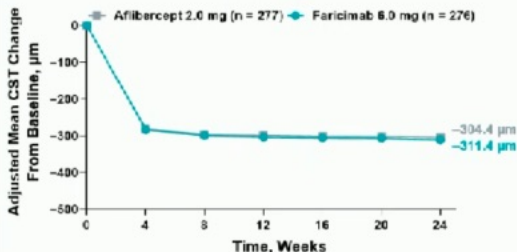
COMINO



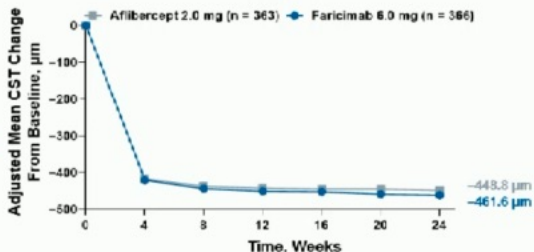
Faricimab Achieved Robust Reductions in CST Across Studies Results Were Comparable Between Treatment Arms

ITT Population

BALATON (BRVO)



COMINO (H/CRVO)



Faricimab Was Well Tolerated, With a Safety Profile Similar to That of Aflibercept

	BALATON (BRVO)		COMINO (H/CRVO)	
	Aflibercept 2.0 mg n = 274	Faricimab 6.0 mg n = 276	Aflibercept 2.0 mg n = 351	Faricimab 6.0 mg n = 365
AEs Through Week 24, Patients With ≥ 1 AE, n (%)				
Ocular AEs	56 (20.4%)	45 (16.3%)	100 (27.7%)	84 (23.0%)
Serious ocular AEs	2 (0.7%)	3 (1.1%)	12 (3.3%)	9 (2.5%)
Ocular AEs of special interest	2 (0.7%)	1 (0.4%)	12 (3.3%)	8 (2.2%)
Intraocular inflammation events	0	1 (0.4%)*	4 (1.1%)	8 (2.2%)
Vitreitis	0	0	0	3 (0.8%)
Iritis	0	0	2 (0.6%)	2 (0.5%)
Uveitis	0	0	1 (0.3%)	2 (0.5%) [‡]
Noninfectious endophthalmitis	0	0	1 (0.3%)	0
Iridocyclitis	0	0	0	1 (0.3%)
Endophthalmitis events	0	0	1 (0.3%)	0
Retinal vasculitis events	0	0	0	0
Retinal artery occlusion/embolism[‡]	0	0	2 (0.6%)	3 (0.8%)
Serious nonocular AEs	16 (5.8%)	9 (3.3%)	23 (6.4%)	22 (6.0%)
APTC events	4 (1.5%)	3 (1.1%)	5 (1.4%)	4 (1.1%)
AEs leading to treatment discontinuation through week 24	1 (0.4%)	1 (0.4%)	3 (0.8%)	3 (0.8%)

* Verbalism term "noninflammatory vitreous cells".



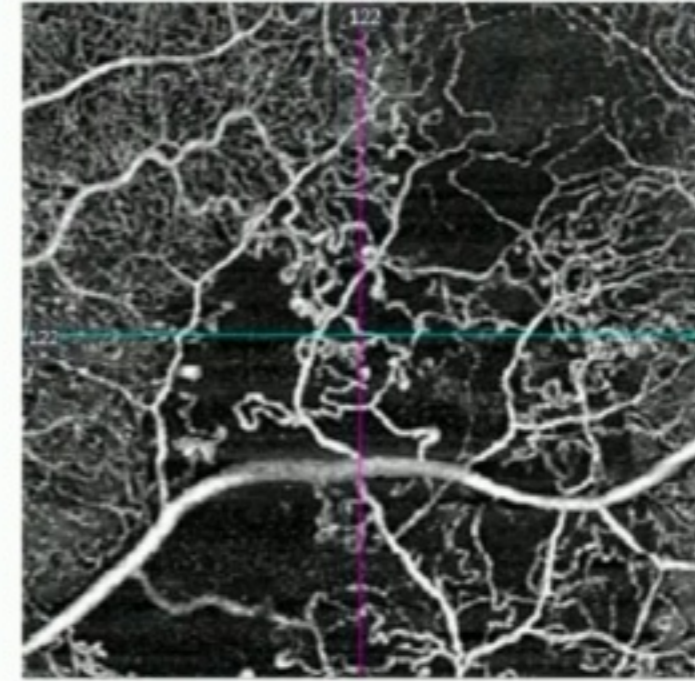
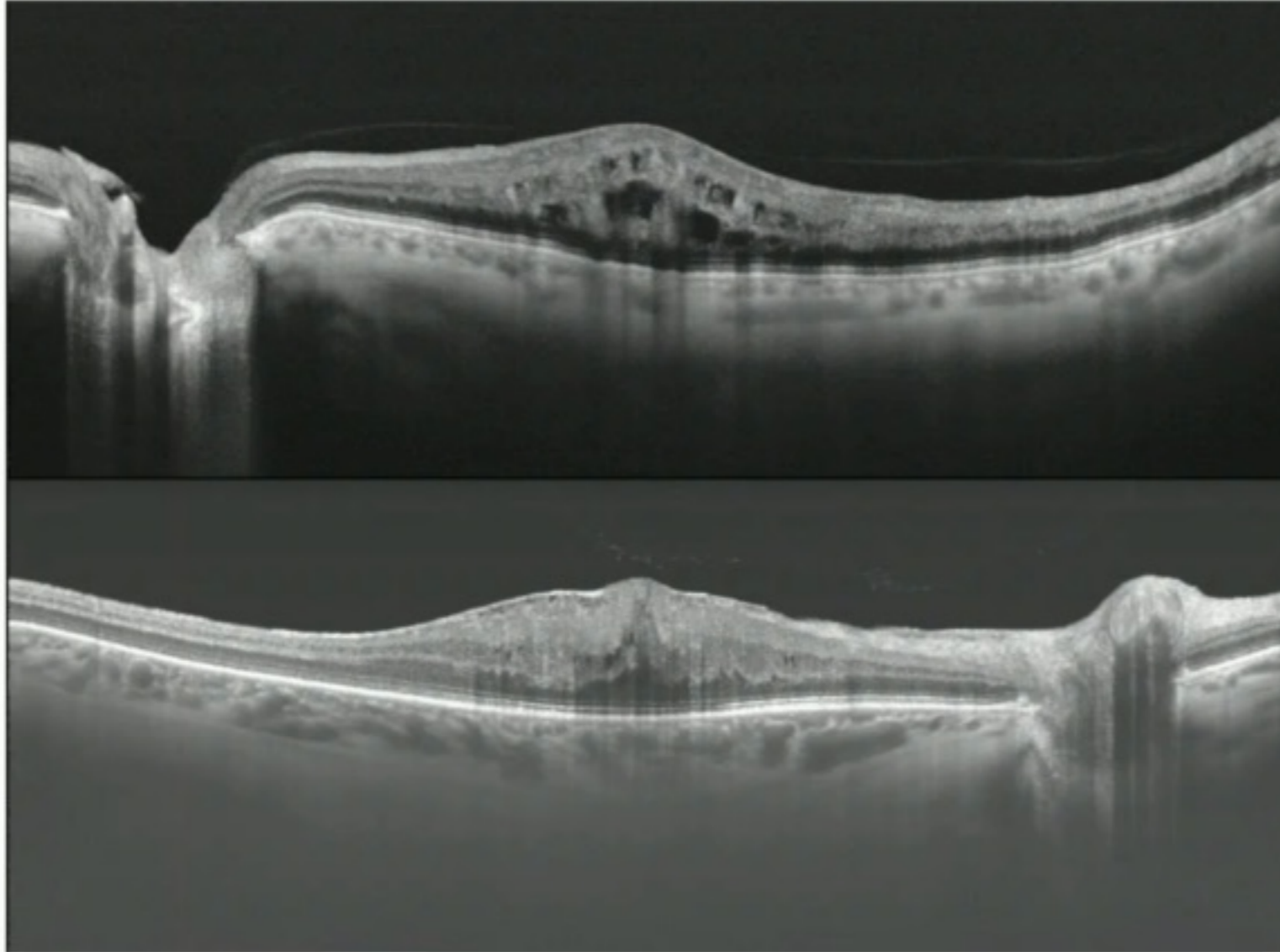
The 10 key messages

1. Systemic evaluation should be minimal
2. At baseline do clinical examination, OCT and FA, continue with clinical examination and OCT. Wide field imaging and OCTA are optional but at this point do not change management
3. Treat early in the course of the disease
4. Non perfusion does not change the way of treatment
5. In case of ME antiVEGF as first line is warranted
6. Some difference between antiVEGFs was shown
7. Ozurdex is a good option in patients unsuitable to antiVEGF or non responders
8. Faricimab should be considered
9. **If neovascularization develops PRP with antiVEGF is warranted**
10. **Visual acuity may be improved even in patients with bad visual acuity at baseline**



Long-term complications and vitrectomy in RVO

Jorge Ruiz-Medrano MD PhD FEBO







Macular epithelium pigment degeneration

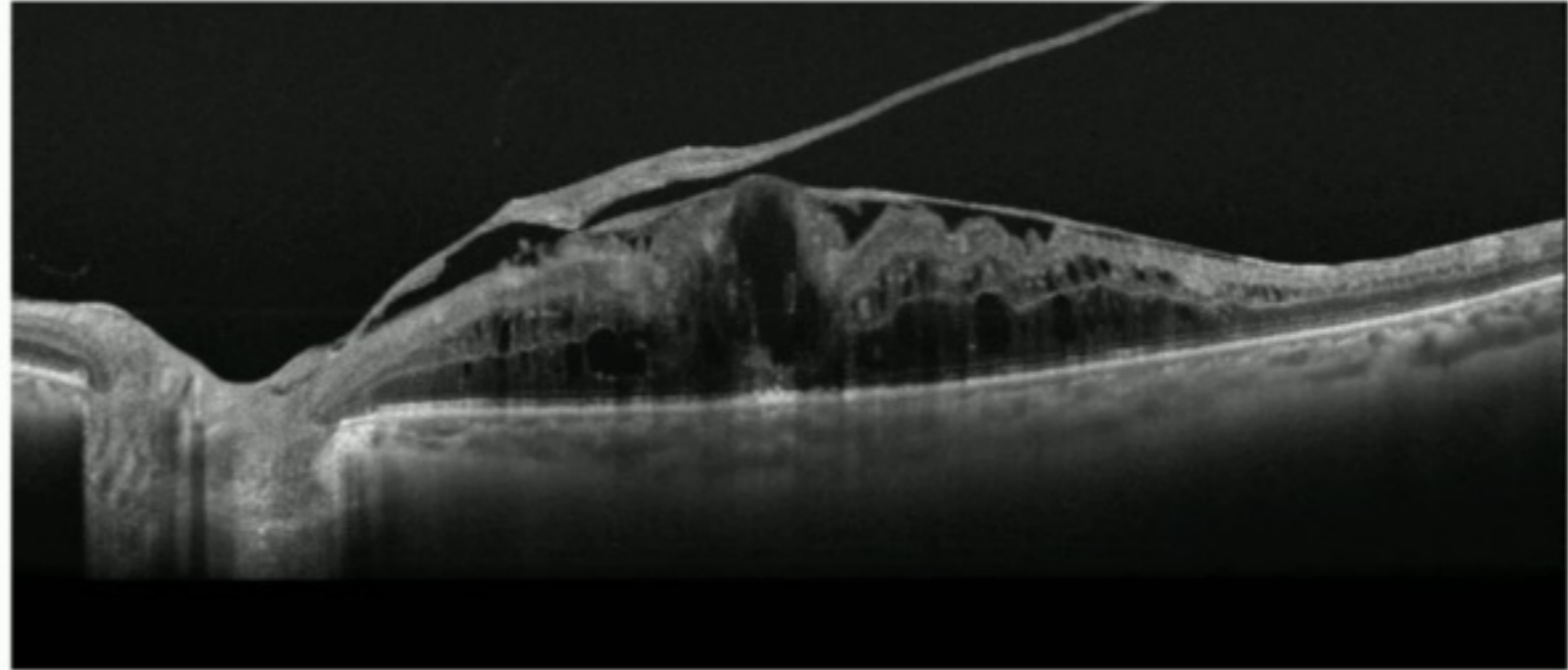
- Within 12 months from onset:
 - 39 % of eyes with ischemic CRVO
 - 21.5 % in nonischemic CRVO
- Within 24 months, 54 and 36 %, respectively
- Moderate/severe macular edema: more likely to have epithelial pigment degeneration and serous macular detachment
- Among eyes with ischemic CRVO, severity of macular edema at initial visit was not significantly associated



Hayreh SS. Am J Ophthalmol. 1994;117(4):429-41.

Epirretinal membrane

- Within 12 months from onset:
 - 12 % in nonischemic CRVO
 - 12.5 % in ischemic CRVO
- 24 months: 19.5 and 25 %, respectively
- Severity of macular edema at initial examination was significantly associated with development of ERM in nonischemic CRVO
- Among eyes with ischemic CRVO, severity of macular edema at the initial visit was not found to be significantly associated



> [Ophthalmol Ther.](#) 2022 Apr;11(2):661-675. doi: 10.1007/s40123-022-00461-7.
Epub 2022 Jan 31.

Epiretinal Membrane Peeling in Eyes with Retinal Vein Occlusion: Visual and Morphologic Outcomes

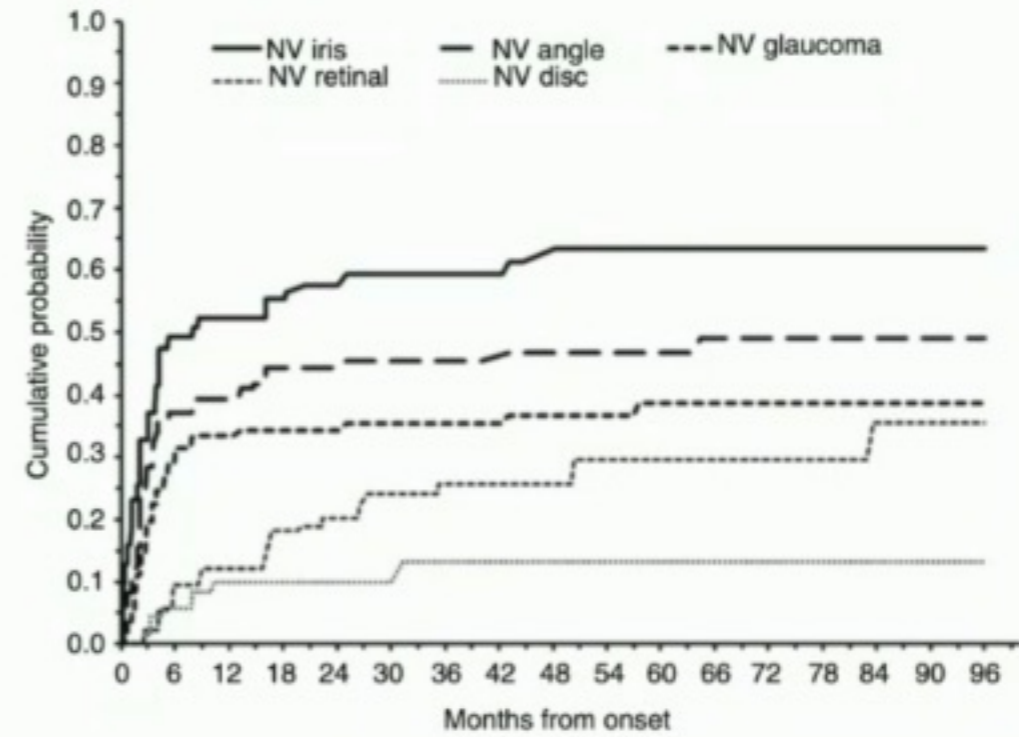
Maria Vittoria Cicinelli ^{1 2}, Irini Chatziralli ³, Sara Touhami ^{4 5}, Anissa Smaoui ^{4 5},
Beatrice Tombolini ⁶, Marco Nassisi ^{7 8}, Panagiotis Theodossiadis ³, Rosangela Lattanzio ⁶,
Francesco Bandello ^{9 6}

Results: Twenty-one eyes of 21 patients with a median follow-up of 18 months were included. The BCVA improved significantly after ERM peeling (baseline vs. 24 months, $p = 0.01$). Absence of the external limiting membrane/ellipsoid zone on OCT was associated with worse visual outcomes (regression estimate [95% confidence interval, CI] = 0.93 [0.39-1.48] logMAR, $p = 0.004$). Eyes with disorganization of the inner retinal layers at baseline had higher CMT values at each visit (regression estimate [95% CI] = 114.1 [78.9-219.4] μm , $p = 0.004$). Older age at the time of RVO ($p = 0.03$) and branch RVO ($p = 0.04$) were risk factors for persistent macular edema after ERM removal.

Conclusion: PPV and ERM removal provided encouraging functional and morphological results in eyes with RVO, with disappearance of macular edema in most eyes. The integrity of the outer retina and preservation of inner retinal segmentation were associated with better visual and anatomical outcomes after ERM removal, respectively.

Optic disc changes

- 38 % of ischemic CRVO and 2 % of nonischemic CRVO in the first year
- Retinociliary collaterals developed in 41.0 % within 12 months in nonischemic CRVO and in 46.5 % in ischemic CRVO
- Giuffre et al. in a study of 94 CRVO eyes, found these collaterals in 30 % after a follow-up of more than 1 year and no difference between nonischemic CRVO and ischemic CRVO.



Hayreh SS. Am J Ophthalmol. 1994;117(4):429-41.

> [Clin Ophthalmol.](#) 2011;5:1089–93. doi: 10.2147/OPTH.S23164. Epub 2011 Aug 5.

Pars plana vitrectomy and internal limiting membrane peeling for macular edema secondary to retinal vein occlusion

[Nader Baharivand](#)¹, [Amirhossein Hariri](#), [Alireza Javadzadeh](#), [Ebadollah Heidari](#), [Karim Sadegi](#)

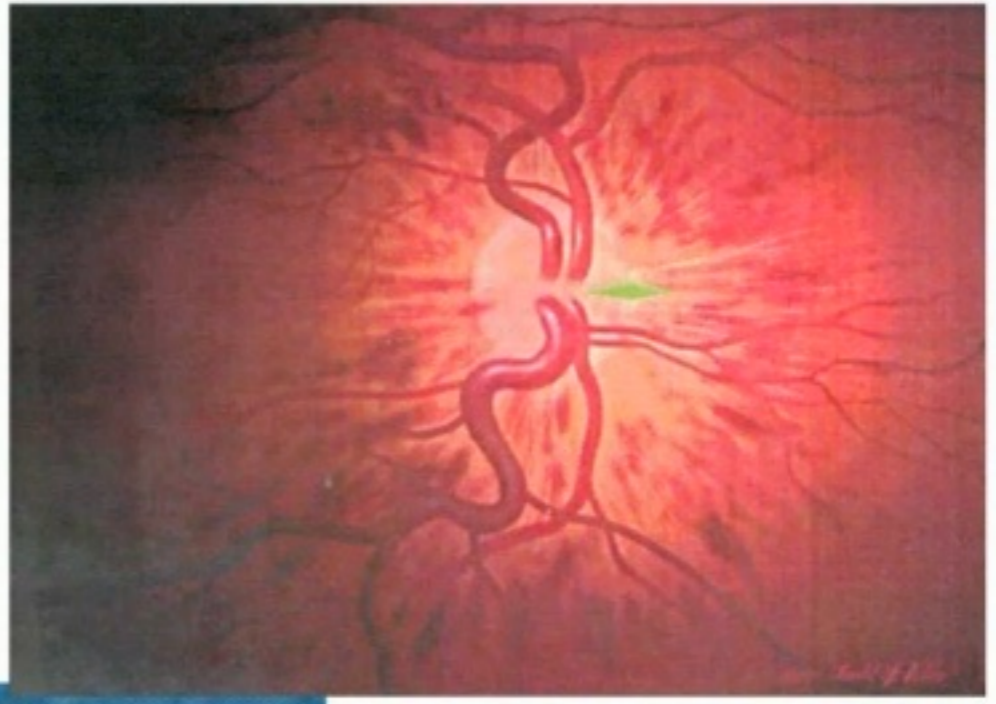
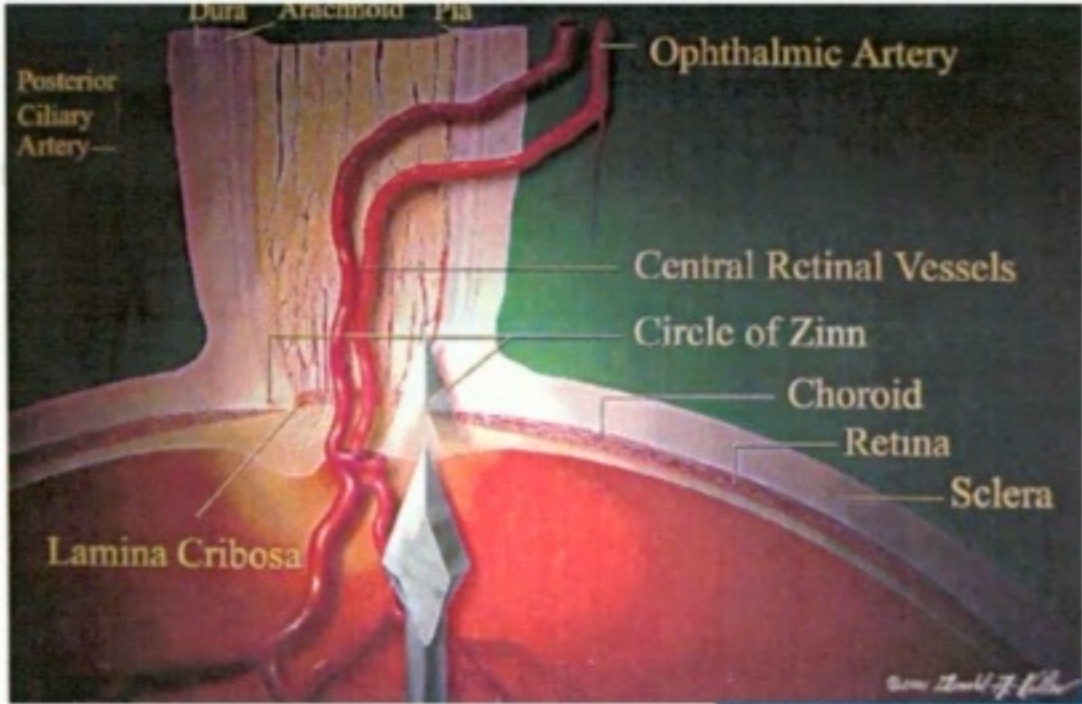
Conclusion: In eyes with macular edema secondary to RVO, pars plana vitrectomy with internal limiting membrane peeling can resolve macular edema, but the improvement in BCVA was not statistically significant in this study.

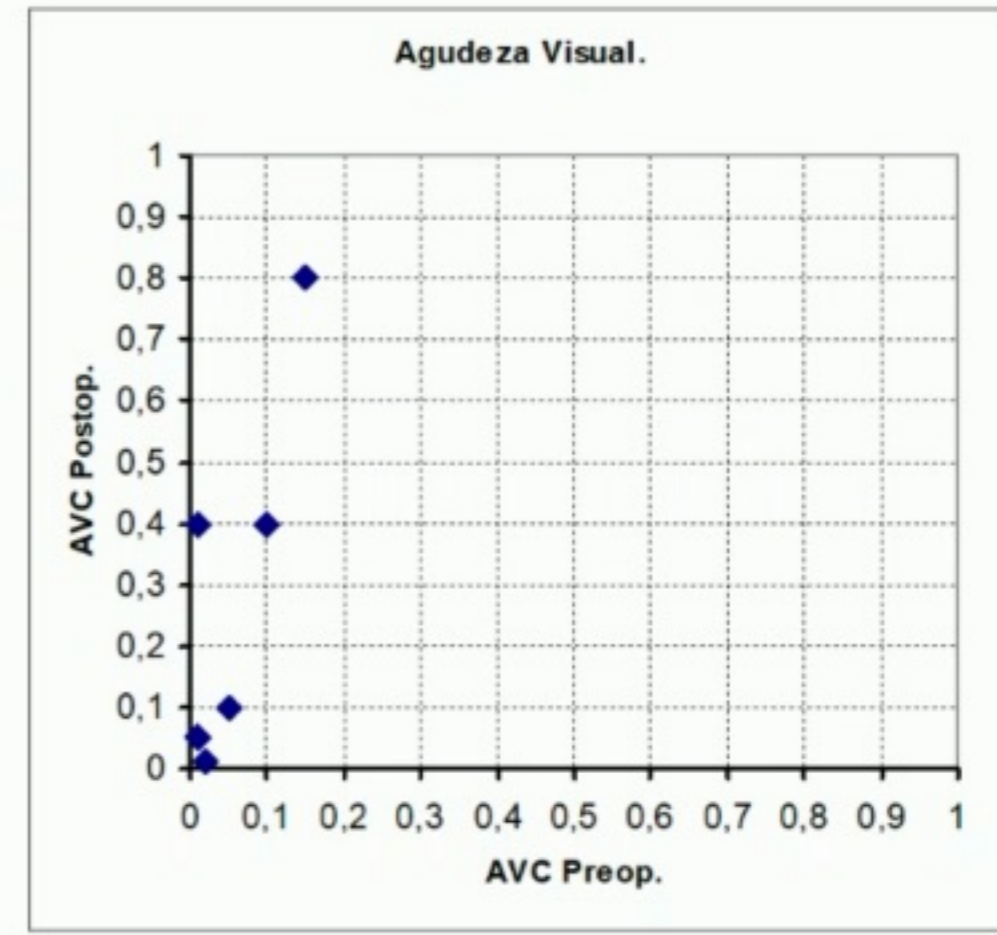
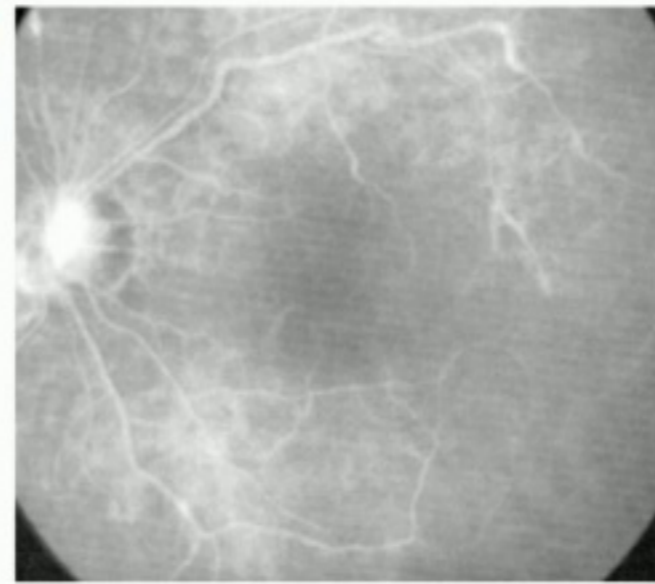
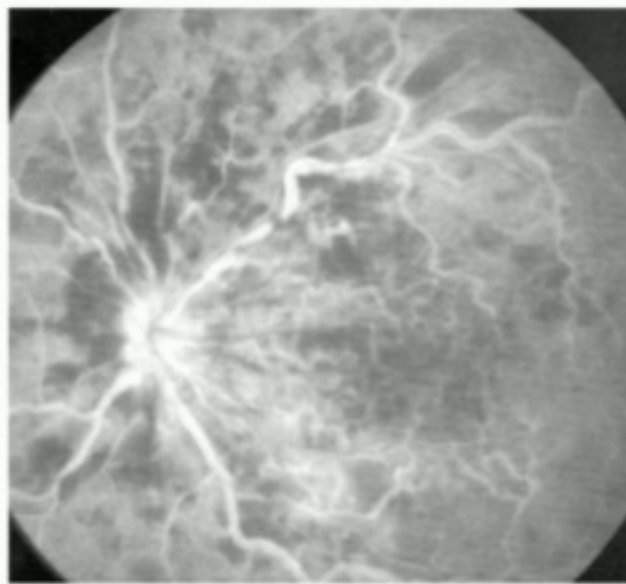
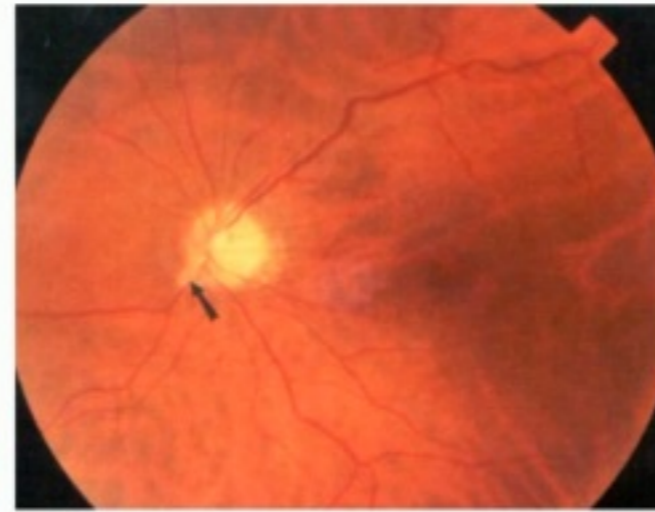
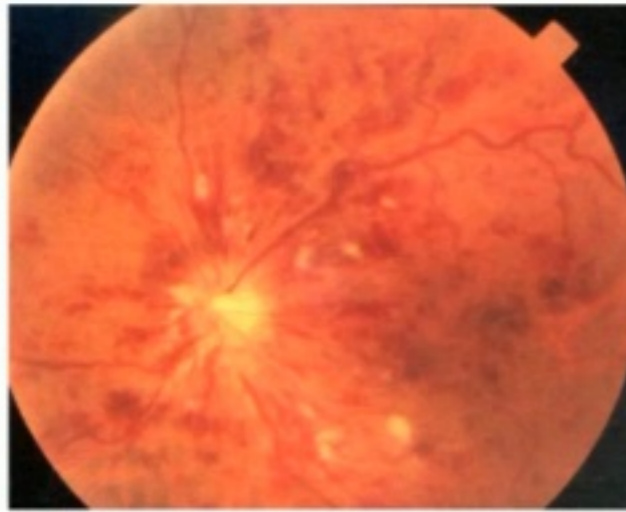
> [Eur J Ophthalmol.](#) 2009 Nov-Dec;19(6):1055–62. doi: 10.1177/112067210901900625.

Pars plana vitrectomy with ILM peeling for macular edema secondary to retinal vein occlusion

[Marzena Raszewska-Steglinska](#)¹, [Piotr Gozdek](#), [Slawomir Cisiecki](#), [Zofia Michalewska](#), [Janusz Michalewski](#), [Jerzy Nawrocki](#)

Conclusions: PPV with ILM peeling may improve anatomic and functional prognosis in patients with macular edema secondary to RVO. Vitrectomy with ILM peeling seems to be beneficial for macular edema secondary to RVO in patients treated within 1 month from the onset of symptoms. PPV with ILM peeling in ischemic RVO and nonischemic RVO improves visual acuity.





> [Retina](#). 2004 Aug;24(4):530-40. doi: 10.1097/00006982-200408000-00005.

Management of macular edema in branch retinal vein occlusion with sheathotomy and recombinant tissue plasminogen activator

Jose García-Arumí ¹, Vicente Martínez-Castillo, Ana Boixadera, Hugo Blasco, Borja Corcostegui

Methods: Arteriovenous sheathotomy was performed, using a bimanual technique, followed by fluid-air exchange and injection of 25 mg of recombinant tPA over the area of the occluded vein.

Results: Intraoperative sectioning of the common arteriovenous sheath was achieved in all 40 patients. Thrombus release was observed in 11 cases (27.5%) and was correlated with early surgery ($P < 0.001$) and better final visual recovery ($P < 0.06$). Optical coherence tomography showed macular thickness that decreased by greater than 40% in 31 patients (77.5%) compared with preoperatively, and correlated to postoperative visual acuity ($P < 0.001$). The mean visual acuity increased from 20/100 to 20/40, with 70% of patients gaining three or more lines of visual acuity (Pearson 0.378, $P = 0.016$).

Conclusion: Surgical venous decompression and injection of recombinant tPA may effectively manage macular edema secondary to BRVO, thus improving anatomic and visual outcome. Early surgical intervention may obtain maximum final visual recovery.

> [Retina](#). 2023 Sep 1;43(9):1506-1513. doi: 10.1097/IAE.0000000000003839.

VITRECTOMY FOR VITREOUS HEMORRHAGE ASSOCIATED WITH RETINAL VEIN OCCLUSION: Visual Outcomes, Prognostic Factors, and Sequelae

Taku Wakabayashi ¹, Neil Patel ², Matthew Bough ², Ankur Nahar ², Young Sheng ²,
Bita Momenaei ¹, Mirataollah Salabati ¹, RaziyeH Mahmoudzadeh ¹, Ajay E Kuriyan ¹,
Marc J Spirn ¹, Allen Chiang ¹, Jason Hsu ¹, Mitchell S Fineman ¹, Carl D Regillo ¹,
Arunan Sivalingam ¹, Allen C Ho ¹, Omesh P Gupta ¹, Yoshihiro Yonekawa ¹

> **Ref Purpose:** To report the outcomes of pars plana vitrectomy for vitreous hemorrhage (VH) associated with retinal vein occlusion and to identify prognostic indicators. 9.

VI] Methods: Interventional, retrospective consecutive case series between 2015 and 2021.

AS Results: The study included 138 eyes of 138 patients (64 female and 74 male); 81 patients had branch retinal vein occlusion and 57 had central retinal vein occlusion. The mean age was 69.8 years. The mean duration between the diagnosis of VH and surgery was 79.6 ± 115.3 (range, 1-572) days. The mean follow-up was 27.2 months. The logarithm of the minimum angle of resolution visual acuity significantly improved from 1.95 ± 0.72 (Snellen equivalent, 20/1782) to 0.99 ± 0.87 (20/195) at 6 months and to 1.06 ± 0.96 (20/230) at the final visit (both $P < 0.001$). The visual acuity at 6 months improved by three or more lines in 103 eyes (75%). Postoperative complications during follow-up included recurrent VH in 16 eyes (12%) (of which 8 eyes underwent reoperations), rhegmatogenous retinal detachment in six eyes (4%), and new neovascular glaucoma in three eyes (2%). Worse final visual acuity was significantly associated with older age ($P = 0.007$), concurrent neovascular glaucoma ($P < 0.001$), central retinal vein occlusion ($P < 0.001$), worse preoperative visual acuity ($P < 0.001$), postoperative new neovascular glaucoma ($P = 0.021$), and postoperative retinal detachment ($P < 0.001$). The duration of VH was not associated with visual outcomes ($P = 0.684$). Preoperative antivascular endothelial growth factor injections and tamponade did not prevent postoperative recurrent VH.

Taku
Bita
Marc
Aruni

Conclusion: Pars plana vitrectomy is effective for VH associated with retinal vein occlusion, regardless of the duration of hemorrhage. However, pre-existing risk factors and postoperative sequelae may limit visual recovery.

SE
ION:
sequelae

Sheng²,
Uriyan¹,
gillo¹,

