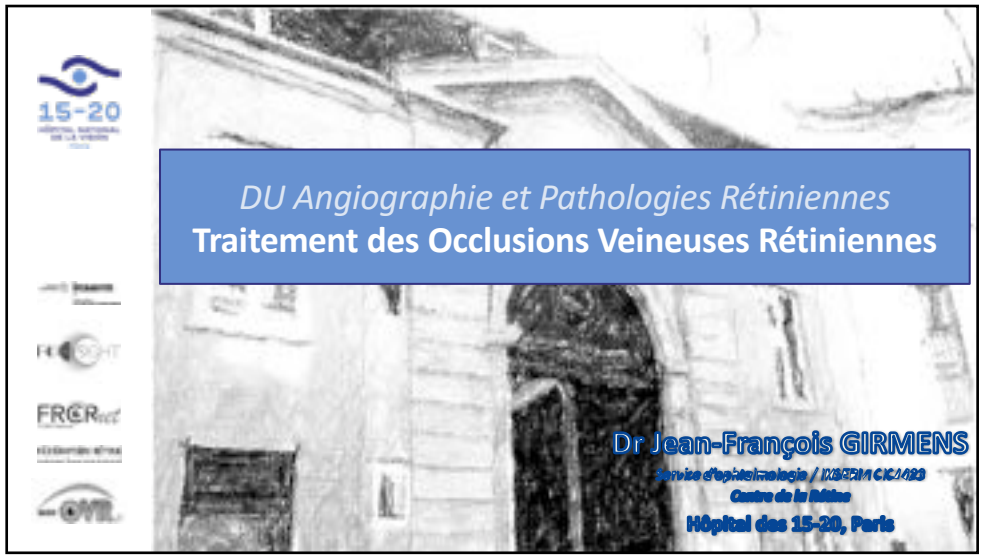


DU Angiographie et Pathologies Rétiniennes

Traitement des Occlusions Veineuses Rétiniennes

Dr Jean-François GIRMENS

Service d'ophtalmologie / INSERM CIC 1423

Centre de la Rétine

Hôpital des 15-20, Paris

1

2 aspects

Traitement « étiologique »

- Améliorer la circulation veineuse
  - Traitement systémique ?
    - Hémodilution ?
  - Chirurgie ?

Prise en charges des complications

- Ischémie rétinienne
  - Rubéose irienne
    - GNV
  - NV pré-rétiniens
- Œdème maculaire
  - Laser ?
  - Injections intra-vitréennes ?
  - Est-ce une urgence ?

2

Traitement de l'occlusion

AMÉLIORER LA CIRCULATION RÉTINIENNE ?

3

Traitement en phase aigüe ?

Médical ?

- Antiagrégants plaquettaires
- Correcteurs rhéologiques (troxérutine, pentoxifylline)
- Hypotonisant oculaires
- Anticoagulants
- Fibrinolyse

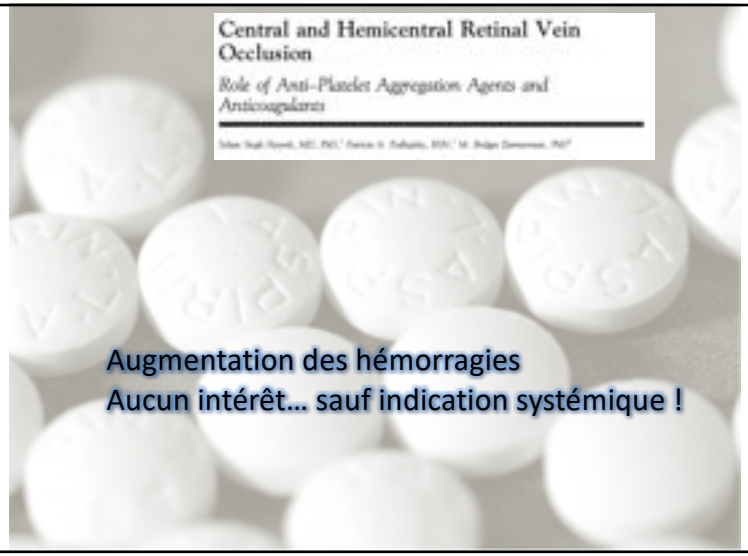
- Hémodilution

Chirurgical et laser ?

- Neurotomie radiaire
- Adventicectomie
- Fibrinolyse in-situ

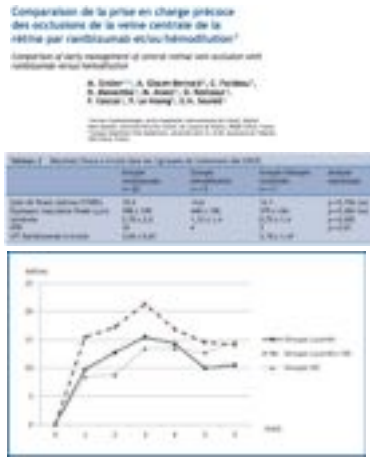
- (Anastomoses rétino-choroïdiennes laser)

4

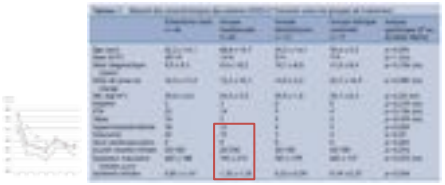


5

Hémodilution vs anti-VEGF

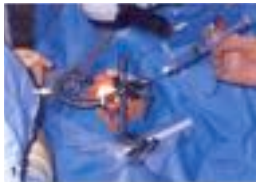


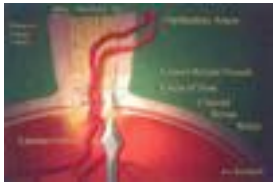
- Fév 2010 – juin 2013
  - multicentrique, prospective, randomisée
- 44 patients (18 -75 a)
  - OVCR < 1mois
  - AV < 20/40
  - Hématocrite ≥ 38%



6

Approches chirurgicales…





JAMA Ophthalmology | Original Investigation

Two-Year Efficacy of Ranibizumab Plus Laser-Induced Chorioretinal Anastomosis vs Ranibizumab Monotherapy for Central Retinal Vein Occlusion
A Randomized Clinical Trial

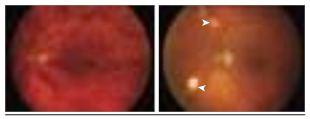


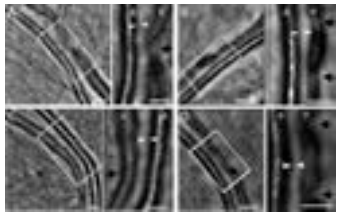
Table 2. Treatment Exposure[a]

Phase	No. of Injections, Mean (95% CI)		Count Ratio (95% CI)	P Value
	Combination Group (n = 29)	Ranibizumab Alone Group (n = 29)		
Loading phase (month 1 to month 6)	5.5 (4.7-6.5)	5.7 (4.9-6.7)	0.96 (0.77-1.20)	.74
Total maintenance phase (month 7 to month 24)	3.2 (2.5-3.8)	7.1 (6.0-8.0)	0.46 (0.36-0.61)	<.001
Early maintenance phase (month 7 to month 11)	1.5 (1.1-2.0)	2.4 (1.9-3.1)	0.60 (0.41-0.88)	.01
Late maintenance phase (month 13 to month 24)	1.7 (1.3-2.2)	4.6 (3.8-5.5)	0.37 (0.26-0.51)	<.001

7

Imagerie à haute résolution (OA)

- Déformation de la veine sans contact des parois artérielle et veineuse
  - engainement fibreux au sein de l'adventice commune aux deux vaisseaux ?



- OVCR : localisation précise et nature de l'obstacle (NO) ?

8

Au total : pas de recommandation avec haut niveau de preuve

Therapies for Macular Edema Associated with Central Retinal Vein Occlusion

A Report by the American Academy of Ophthalmology

Steven Yeh, MD,[1] Stephen J. Kim, MD,[2] Allen C. Ho, MD,[3] Scott D. Schoenberger, MD,[4] Sophie J. Bakri, MD,[5] Justis P. Ehlers, MD,[6] Jennifer E. Thorne, MD, PhD[7]

Ophthalmology 2015 / 2017

Ophthalmologica

Guidelines

Ophthalmologica
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Published online: August 14, 2019

Therapies for Macular Edema Associated with Branch Retinal Vein Occlusion

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Justis P. Ehlers, MD,[1] Stephen J. Kim, MD,[2] Steven Yeh, MD,[3] Jennifer E. Thorne, MD, PhD,[4] Prithvi Mruthyunjaya, MD, MHS,[5] Scott D. Schoenberger, MD,[6] Sophie J. Bakri, MD[7]

Guidelines for the Management of Retinal Vein Occlusion by the European Society of Retina Specialists (EURETINA)

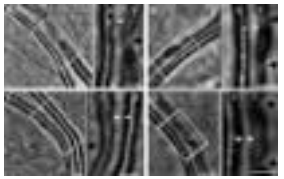
Ursula Schmidt-Erfurth[a] José Garcia-Arumi[b] Bianca S. Gerendas[a] Edoardo Midena[c] Sobha Sivaprasad[d] Ramin Tadayoni[e] Sebastian Wolf[f] Anat Loewenstein[g]

[a]Department of Ophthalmology, Medical University of Vienna, Vienna, Austria; [b]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [c]Department of Ophthalmology, University of Padua, Padua, Italy; [d]Moorfields Eye Hospital NHS Foundation Trust, London, UK; [e]Department of Ophthalmology, Lariboisière Hospital Paris, Paris, France; [f]Department of Ophthalmology, Inselspital, University of Bern, Bern, Switzerland; [g]Department of Ophthalmology Tel Aviv Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Ophthalmologica. 2019;242(3):123-162

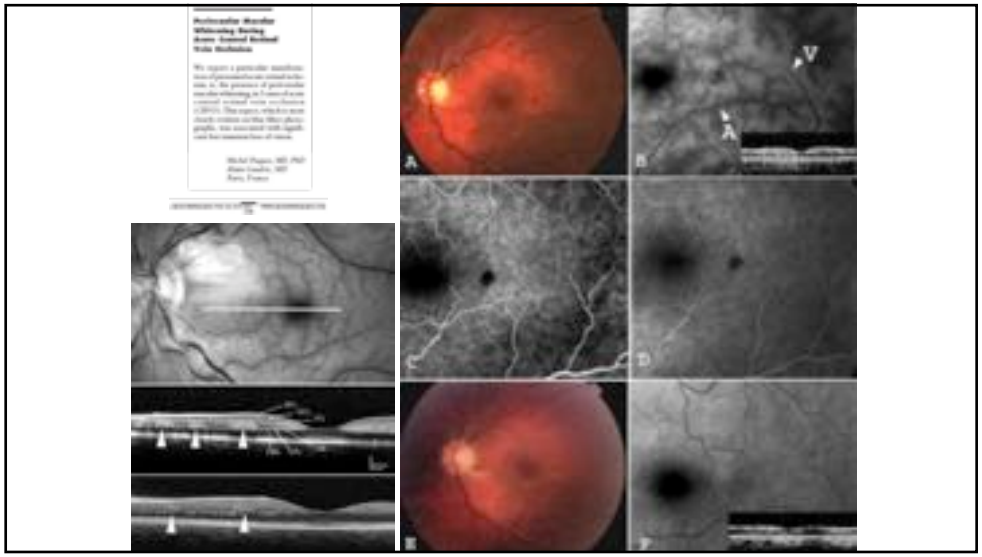
Nouvelles pistes ?

- Atteinte de la paroi vasculaire ?
- Voie MEK ?



- Augmentation de l'adhérence des globules rouges à l'endothélium vasculaire
  - surexpression membranaire de phosphatidylsérine

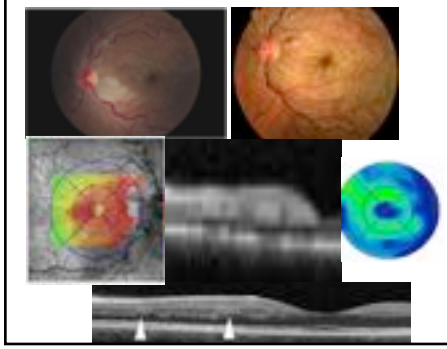
  - Essai ouvert de phase 2 : hydroxycarbamide PO



Intérêt d'une nouvelle classification des OVR

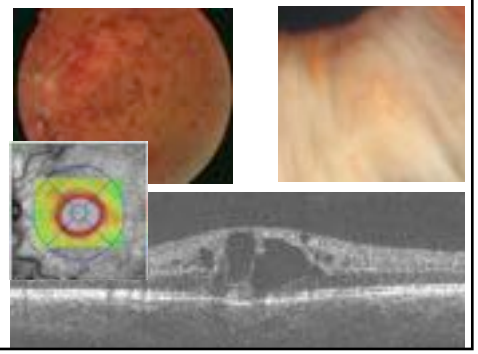
Type A

- Bas débit aigu
  - +/- œdème papillaire



Type B

- Début insidieux
  - œdème maculaire

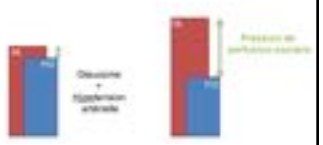


Intérêt d'identifier les types « A »

- Contre-indication aux injections ?

risque d'aggravation de la situation hémodynamique

- Tenter d'augmenter la pression de perfusion oculaire ?
  - traitement hypotonisant local
    - même en l'absence d'HTO
  - si TAs <120 mmHg, augmentation temporaire ?
    - interruption d'un traitement anti-hypertenseur
    - sel ?
    - Activité physique
- Prise en charge d'une éventuelle anémie



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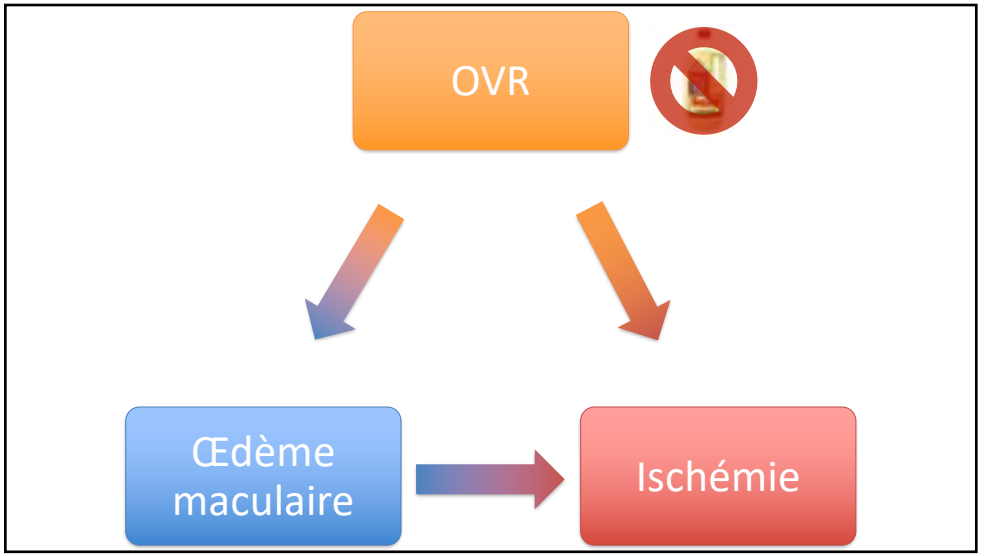

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GLAUCOME NÉO-VASCULAIRE : COMPLICATION REDOUTÉE DES OVCR ISCHÉMIQUES

15

Risque d'ischémie

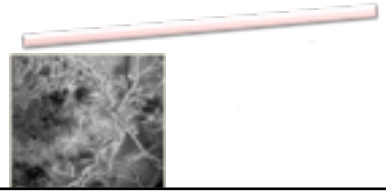
30 à 50% des formes initialement bien perfusées vont évoluer vers une forme ischémique

dont 18% évolueront vers la rubéose irienne
voire le glaucome néovasculaire

16

Limites de la classification angiographique

- **Perfusion ≠ Ischémie**
  - Ischémie = souffrance cellulaire
  - Perfusion = vascularisation capillaire
- Parfois difficile initialement
  - Masquage /hémorragies
- Peu de valeur pronostique
- Définition variable de « l'ischémie »
  - 10DP ? 30 DP?
  - Champs étudiés (7/9 champs ? « Wide-field » ?)



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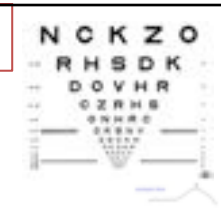
Intérêt des signes fonctionnels…

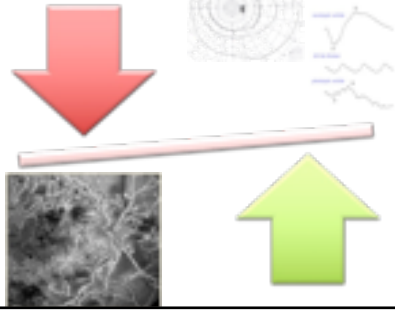
Major review

Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion

Meiaad Khayat, MBBS, MSc[a,b], Michael Williams, BMedSci, MD, MRCOphth, MMedEd[c], Noemi Lois, MD, PhD, FRCS(Ed), FRCOphth[a,]*

[a] Wellcome-Wolfson Institute for Experimental Medicine, School of Medicine, Dentistry & Biomedical Sciences, Queen's University Belfast, Belfast, Northern Ireland, United Kingdom
[b] Department of Anatomy, College of Medicine-Rabigh Branch, King Abdulaziz University, Rabigh, Saudi Arabia
[c] Center for Medical Education, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, Northern Ireland, United Kingdom



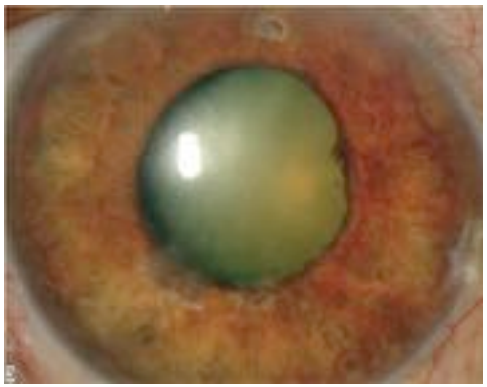


Survey of Ophthalmology 2018;63:816–50

18

… et de l'examen de l'iris +++

- Avant le stade de rubéose irienne…



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Avant le stade de rubéose irienne…

- Diminution du Réflexe Pupillaire Afférent

Pupillary examination	RAPD ≥ 0.6 log unit	Sensitivity 83%; Specificity 70%	Bloom et al., 1993[91]
	RAPD ≥ 0.7 log unit	Sensitivity 88%; Specificity 90%	Hayreh et al., 1990[110]
	PAPD ≥ 0.9 log unit	Sensitivity 80%; Specificity 97%	Hayreh et al., 1990[110]
	RAPD ≥ 1.2 log unit	All eyes with ocular NV and/or extensive retinal CNP had RAPD of ≥1.2 log units ND	Servias et al., 1986[111]

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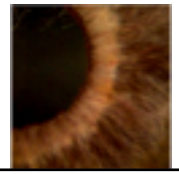
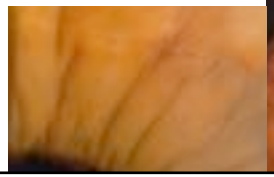
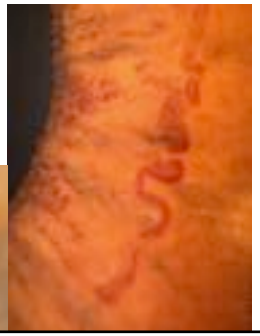
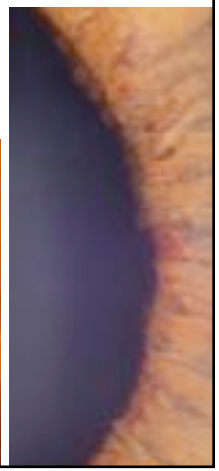
Avant le stade de rubéose irienne…

- DPAR
- Signes précurseurs/précoces de rubéose
  - – Avant dilatation +++
    - Reconvoquer le patient si nécessaire
  - – Fort grossissement
    - Dilatation des vaisseaux radiaires
    - Reperfusion de la collerette
    - Dilatations microanévrysmales

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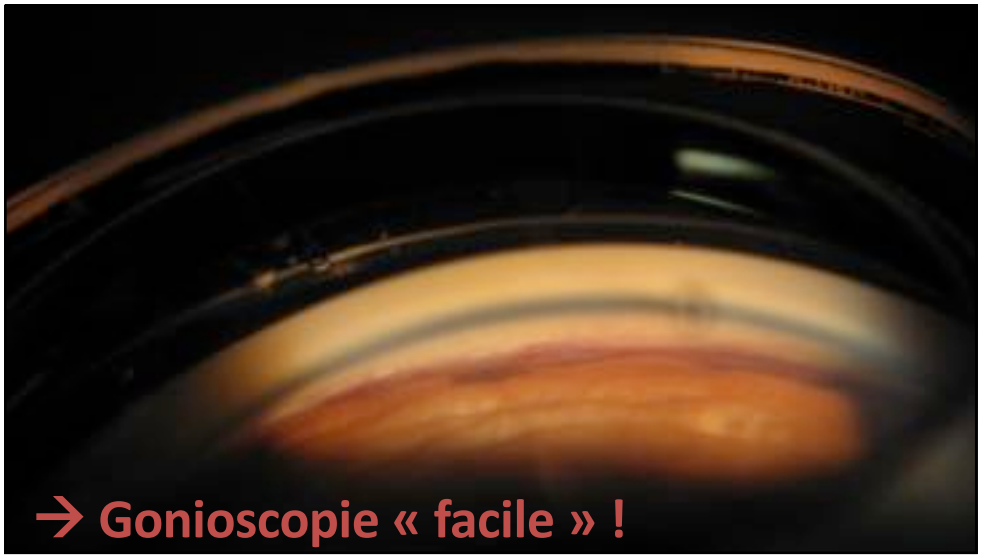

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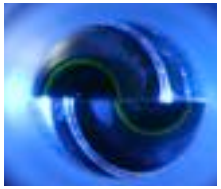
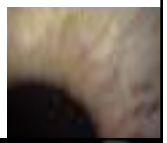
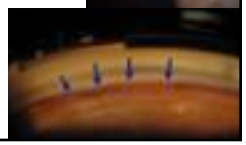
Pour toute OVCR récente (< 6 mois)…

- **Surveillance tous les mois (si Ø anti-VEGF)**
  - au moins pendant les 3-4 premiers mois d'évolution
  - et/ou jusqu'à stabilisation
  - – ⚠ Risque +++ ⚠ :
    - **Arrêt des anti-VEGF** et sous corticoïdes
    - Diabète, âge
    - AV<1/10
    - Nodules cotonneux inter-papillo-maculaires
    - OMC majeur
    - non-perfusion (Index ischémique ?), PPR incomplète

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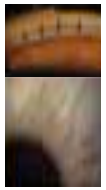
TRAITEMENT DES FORMES ISCHÉMIQUES = PPR

24

La PPR est efficace :

- En présence de néovascularisation débutante
  - Pour éviter le GNV
- En cas d'apparition de NV pré-rétiniens (OBVR)

- En prévention de la néovascularisation si ischémie étendue
  - AV < 1/10
  - Abolition du reflexe pupillaire afférent
  - Scotome central absolu
  - Territoires étendus de non-perfusion



Hayreh SS, et al. Argon laser panretinal photocoagulation in ischemic central retinal vein occlusion. A 10-year prospective study. Graefes Arch Clin Exp Ophthalmol. 1990;228(4):281-96.

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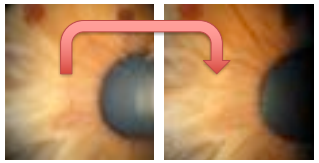
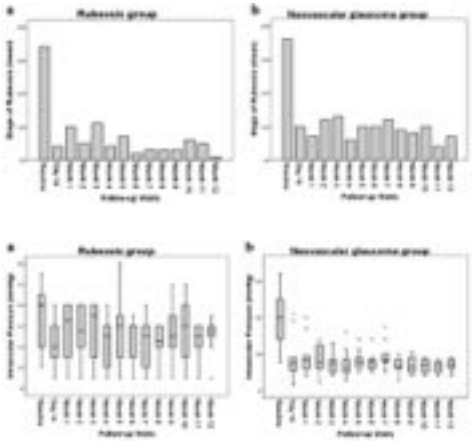
… ± anti-VEGF

- Amélioration rapide de la rubéose



- Diminution rapide de la PIO (GNV)



Graefes Arch Clin Exp Ophthalmol. 2013;251:2403-13

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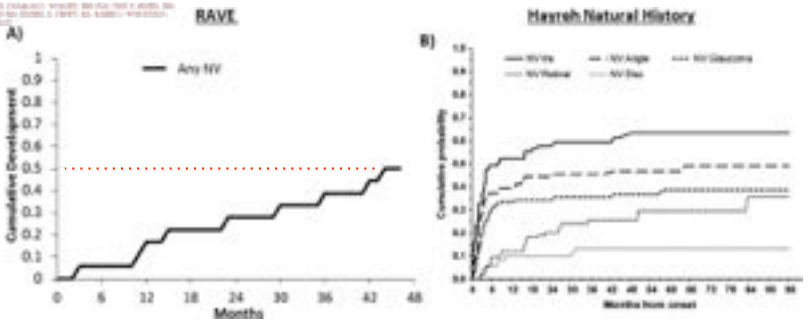
RANIBIZUMAB IN PREPROLIFERATIVE (ISCHEMIC) CENTRAL RETINAL VEIN OCCLUSION

The Rubeosis Anti-VEGF (RAVE) Trial



« […] le risque de complication néovasculaire **n'est pas diminué** par les anti-VEGF seuls, mais **seulement retardé** […] »

Retina. 2014 Sep;34(9):1728-35. doi: 10.1097/IAE.0000000000000191

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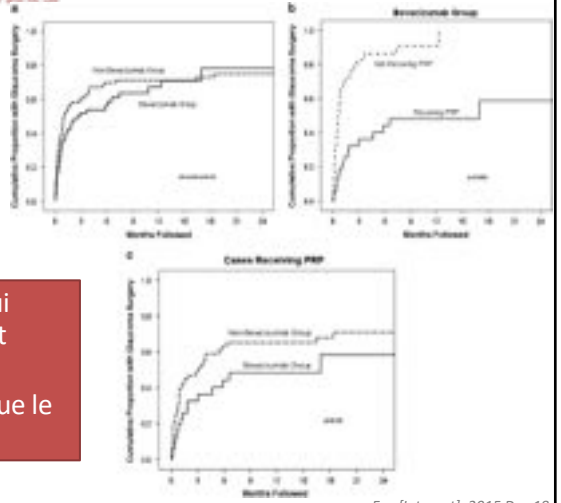
Long-term outcomes of neovascular glaucoma treated with and without intravitreal bevacizumab



« La PPR est **le seul traitement** qui diminue la nécessité de traitement chirurgical d'un GNV, tandis que les anti-VEGF ne font que le **retarder** »

Eye [Internet]. 2015 Dec 18

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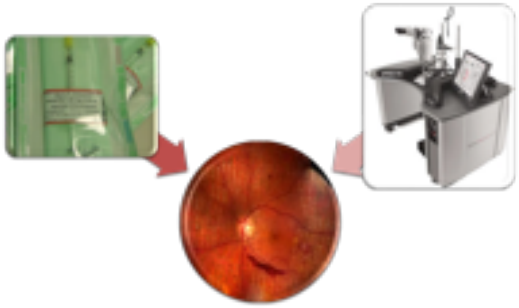
En pratique : traitement combiné, en urgence

- Injection intra-vitréenne d'anti-VEGF
- PPR en une seule séance si possible
  - immédiatement avant
  - ou quelques jours après l'injection
  - dense, jusqu'à l'ora
    - 5 000 à 15 000 impacts



Mesures associées (si GNV) :
- Traitement hypotonisant
- Antalgique
- Anti-inflammatoire

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En pratique : traitement combiné, en urgence

- Injection intra-vitréenne d'anti-VEGF
- PPR en une seule séance si possible
  - immédiatement avant
  - ou quelques jours après l'injection
  - dense, jusqu'à l'ora
    - 5 000 à 15 000 impacts

Mesures associées (si GNV) :
- Traitement hypotonisant
- Antalgique
- Anti-inflammatoire

- **Si PPR impossible / difficile**
  - V3V – endolaser
  - Cryo-application trans-sclérale

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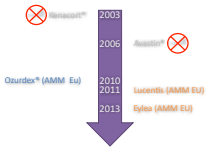
Traitement des complications

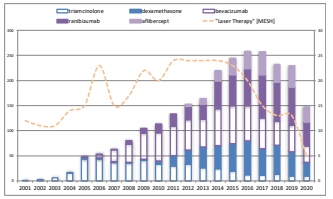
TRAITEMENT DE L'ŒDÈME MACULAIRE

31

Alternatives thérapeutiques

- Laser
  - traitement historique (grille maculaire)
  - nouvelles modalités ?
    - infraliminaire ? ciblé ?
- Injections intra-vitréennes
  - essor relativement récent (AMM)
  - Anti-VEGF vs. corticoïdes
    - ranibizumab vs. aflibercept
- Vitrectomie
- Abstention ?





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… et toujours des questions !

- Faut-il traiter tous les oedèmes maculaires ?
  - On traite une BAV due à un OM
  - Tous les OM ne sont pas identiques
- Le traitement est-il urgent ?
  - Reste-t-il utile tardivement ?
- Quel traitement choisir ?
  - Modalités ?

33

1ère intention = injection(s)…

Ophthalmic Technology Assessment

Therapies for Macular Edema Associated with Central Retinal Vein Occlusion

A Report by the American Academy of Ophthalmology

Steven Yeh, MD,[1] Stephen J. Kim, MD,[2] Allen C. Ho, MD,[3] Scott D. Schwartzberger, MD,[4] Sophie J. Bakri, MD,[5] Justis P. Ehlers, MD,[6] Jennifer E. Thorne, MD, PhD[7]

Conclusions

Review of the available literature suggests that intravitreal anti-VEGF pharmacotherapy is a safe and effective treatment for ME associated with CRVO over 2 years. Intravitreal corticosteroids have also demonstrated efficacy but are associated with higher frequency of adverse effects, including IOP elevation and cataract. Anti-VEGF pharmacotherapy delivered earlier in the course of CRVO favorably affects visual prognosis. Evidence on the safety and efficacy of all other reported interventions (vitrectomy, RON, chorioretinal anastomosis) is of lesser strength.

Ophthalmology 2015;122:769–78. doi:10.1016/j.ophtha.2014.10.013

Prise en charge de l'oedème maculaire secondaire à une occlusion veineuse rétinienne

J Fr Ophtalmol 2015;38:253–63. doi:10.1016/j.jfo.2014.10.003

34

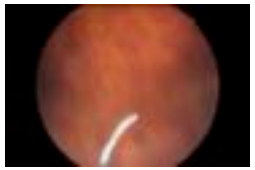
Ozurdex (dexamethasone intravitreal implant) 0.7 mg

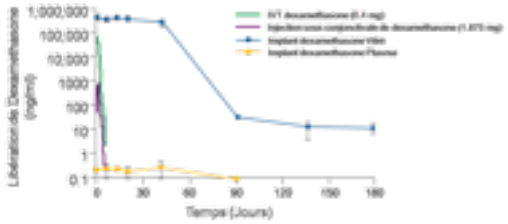
ILUVIEN (fluocinolone acetonide intravitreal implant) 0.19mg

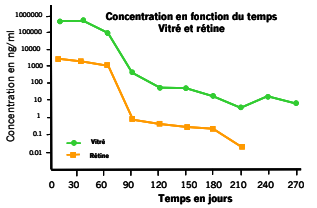
CORTICOÏDES

35

Pharmacocinétique







36

Randomized, Sham-Controlled Trial of Dexamethasone Intravitreal Implant in Patients with Macular Edema Due to Retinal Vein Occlusion

37

Critères d'inclusion / Baseline

	Sham	DEX-PS-DDS 350 µg	DEX-PS-DDS 700 µg
No. of patients (n)	426	414	427
Mean age (years)	63.9	64.9	64.7
Sex (female)	43.7%	46.9%	49.2%
Race (Caucasian)	74.6%	75.4%	75.2%
Diagnosis in study eye:			
CRVO	34.5%	37.2%	31.9%
BRVO	65.5%	62.8%	68.1%
Duration of macular edema (days):			
<90	15.3%	18.4%	16.4%
90–179	51.6%	52.7%	51.3%
≥180	33.1%	29.0%	32.3%
Mean VA (no. of letters [Snellen equivalent])	54.8 (20/80)	53.9 (20/80)	54.3 (20/80)
Mean OCT (µm)	538.6	554.8	562
IOP-lowering medication	3%	5%	6%

38

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1/3 OVCR ; 2/3 OBVR

39

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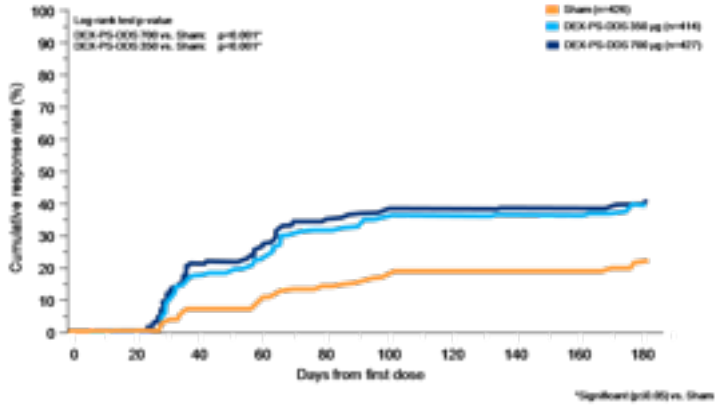
Mean OCT (µm)	538.6	554.8	562
IOP-lowering medication	3%	5%	6%

OM < 3 mois : 15 à 18 %

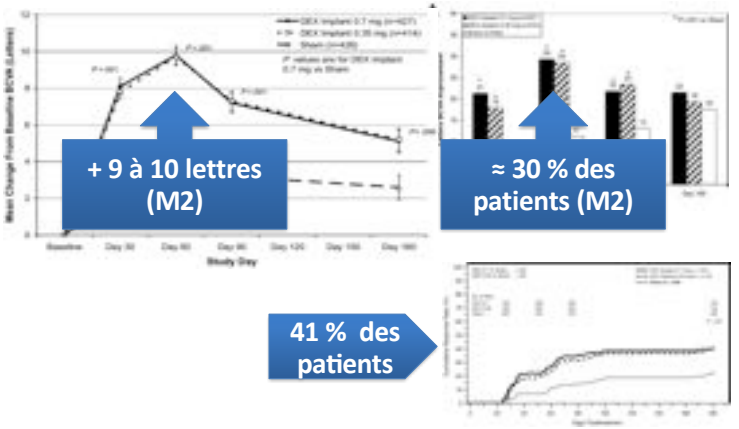
40

« Délai pour atteindre une amélioration de la MAVC ≥15 lettres »



41

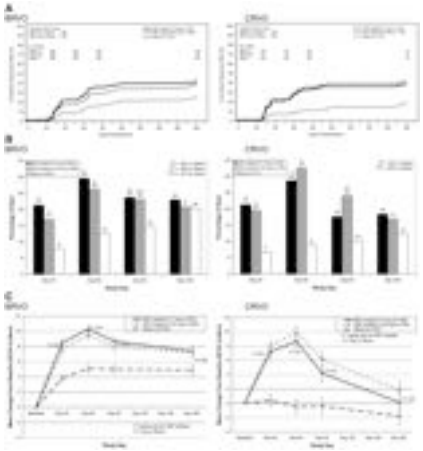
Dexaméthasone : GENEVA (M6)



Haller JA & al. Ophthalmology. 2010 Jun;117(6):1134–46.e3

42

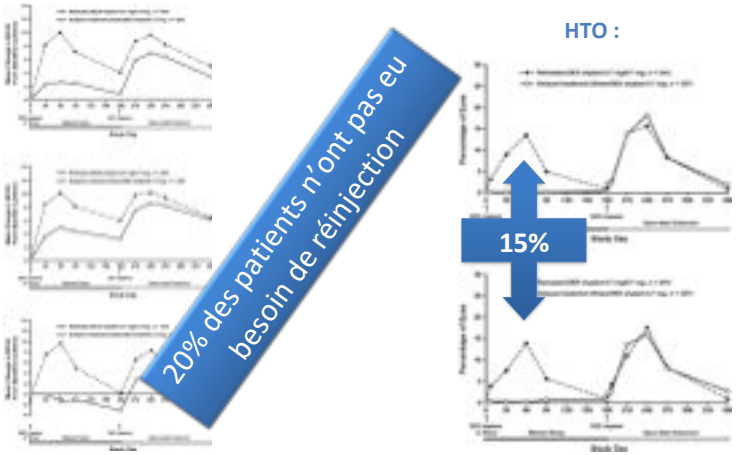
Analyse OVCR/OBVR



Haller JA & al. Ophthalmology. 2010 Jun;117(6):1134–46.e3

43

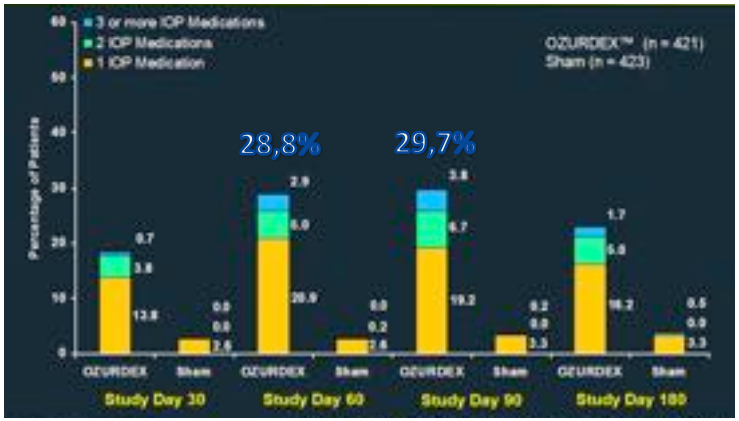
GENEVA (M12)



Haller JA & al. Ophthalmology. 2011 Jul 15;118(12):2453–60

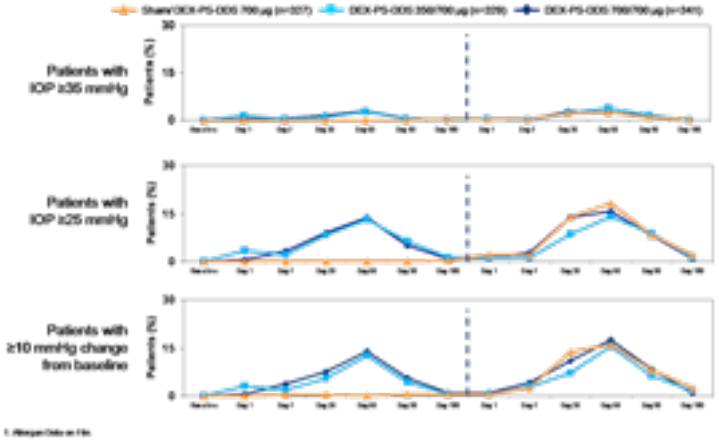
44

Gestion hypertonie



45

Tolérance : PIO (2 injections)



46

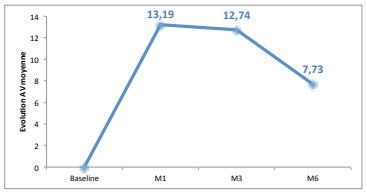
Tolérance : autres

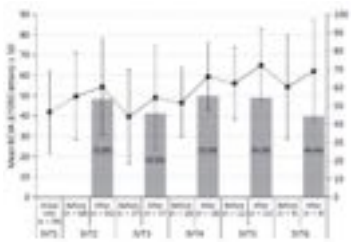
	Sham (n=423)	DEX-PS-DDS 350 µg (n=412)	DEX-PS-DDS 700 µg (n=421)	P-value
Ocular				
Endophthalmie	0	0	0	N/A
Uvéites	0	0	0	N/A
Décollement de rétine	1	0	1	>0.999
Hémorragie vitréenne	6	10	9	0.560
Dommages du cristallin	0	0	0	N/A

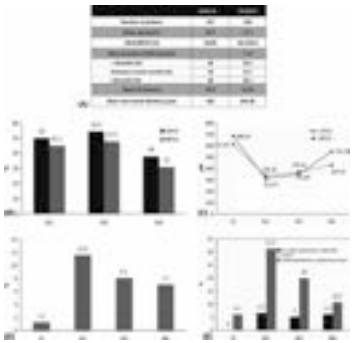
3 (0,9%) chirurgies de cataracte (1 an de suivi…)

47

Ozurdex in the management of the macular edema following retinal vein occlusion in clinical practice (REMIDO/REMIDO2)







Matonti F et al. Acta Ophthalmologica. nov 2013;91(7):e584-6
Pommier S et al. Ophthalmologica. 2016;236(4):186-92

48

Graefes Arch Clin Exp Ophthalmol
DOI 10.1007/s00417-016-3394-y

RETINAL DISORDERS

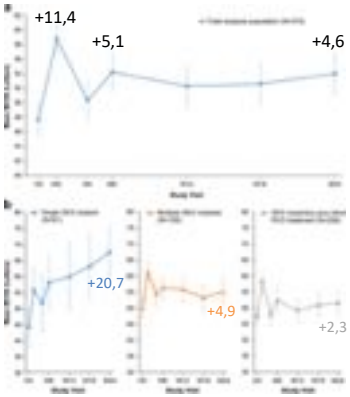
Two-year, prospective, multicenter study of the use of dexamethasone intravitreal implant for treatment of macular edema secondary to retinal vein occlusion in the clinical setting in France

Jean-François Korobelnik[1,2,3] · Laurent Kodjikian[4] · Cécile Delcourt[2,5] · Vincent Gualino[6] · Richard Leaback[6] · Sybil Pinchinat[7] · Marie-Eve Velard[6]

Received: 21 December 2015 / Revised: 25 April 2016 / Accepted: 23 May 2016

2,6 injections en moyenne (tous les 6,6 mois)

Chirurgie cataracte : 40,1 %
HTO (AE) : 34,4 %



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SAFETY OF INTRAVITREAL DEXAMETHASONE IMPLANT (OZURDEX)

The SAFODEX study. Incidence and Risk Factors of Ocular Hypertension

ARIANE MALCLÈS, MD,* CORINNE DOT, MD, PsD,†‡ NICOLAS VOIRIN, PsD,*
ANNE-LAURE VIÉ, MD,* ÉMILIE AGARD, MD,†‡ DAVID BELLOCQ, MD,* PHILIPPE DENIS, MD, PsD,*
LAURENT KODJIKIAN, MD, PsD*

1000 injections
421 yeux, 361 patients
2,4 injections (1-11) par patient
Suivi moyen 16,8 mois (3-55)

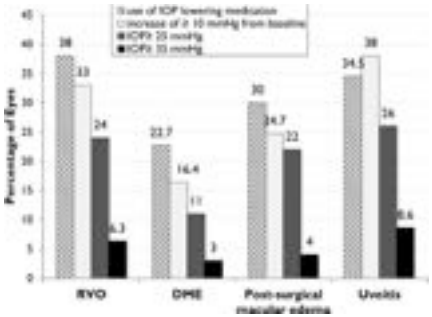


Fig. 1. Percentage of eyes with OHT of ≥25 mmHg, ≥35 mmHg, or an increase of ≥10 mmHg compared with baseline IOP. Percentage of eyes requiring the introduction or addition of IOP-lowering medication during the follow-up period, shown by pathology.

Retina. 2017 Jul;37(7):1352-1359

50

Safety and long-term efficacy of repeated dexamethasone intravitreal implants for the treatment of cystoid macular edema secondary to retinal vein occlusion with or without a switch to anti-VEGF agents: a 3-year experience

Julie Blanc[1] · Clémence Deschasse[1] · Laurent Kodjikian[2] · Corinne Dot[3] · Alain-Marie Bron[1,4] · Catherine Creuzot-Garcher[1,4]

- PPR : 36 patients (54,5%)
- IOP>21mmHg : 36 patients (54,5%)
  - hypoTO : 32 patients (48,5%)
- Chirurgie de cataracte : 70,4% des yeux phakes

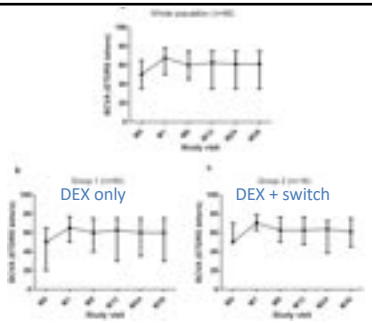


Table 2 Best-corrected visual acuity after repeat dexamethasone intravitreal implants

	DEX 1 ($n=66$)	DEX 2 ($n=62$)	DEX 3 ($n=60$)	DEX 4 ($n=48$)	DEX 5 ($n=38$)	DEX6 ($n=26$)	DEX 7 ($n=17$)	DEX 8 ($n=9$)	DEX 9 ($n=3$)	DEX 10 ($n=2$)
BCVA before DEX implant	50.0 [35.0; 65.0]	52.5 [35.0; 65.0]	55.0 [35.0; 65.0]	50.0 [27.5; 70.0]	60.0 [27.5; 70.0]	50.0 [40.0; 65.0]	50.0 [20.0; 65.0]	60.0 [50.0; 65.0]	65.0[55.0; 85.0]	68.5 [60.0; 77.0]
BCVA after DEX implant	67.5 [50.0; 78.0]	65.0 [50.0; 77.0]	65.0 [45.0; 75.0]	60.0 [35.0; 75.0]	58.5 [40.0; 77.0]	60.0 [30.0; 77.0]	60.0 [25.0; 70.0]	70.0 [35.0; 77.0]	82.0 [77.0; 85.0]	79.5 [77.0; 82.0]
P value	*< 0.001*	*< 0.001*	*< 0.001*	*< 0.001*	*< 0.001*	0.164	0.830	*0.020*	0.165	0.180

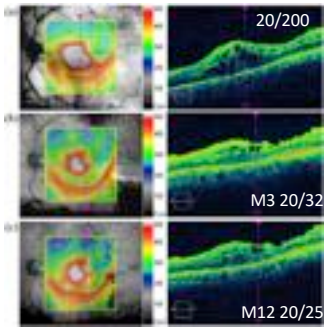
Continuous variables are displayed as median [IQR]; statistically significant *P* values are in italics. BCVA is 4 weeks to 6 weeks after DEX implant
BCVA, best-corrected visual acuity (ETDRS letters); *DEX 1*, first DEX implant; *DEX 2*, second DEX implant, etc.

Graefe's Arch Clin Exp Ophthalmol 2018;256(8):1441-1448. doi:10.1007/s00417-018-4016-7

51

Fluocinolone (Iluvien®) ?

- 1 essai clinique de phase 2
  - 20 patients randomisés (0,2µg / 0,5µg)
    - Dont 11 n'ont pas terminé l'essai !
- 1 cas clinique…
  - Après 6 Ozurdex + pelage MEM
    - Pseudophake
    - Brimonidine + timolol



Therapeutic Advances in Ophthalmology — *Case Report*

Long-term management of non-ischemic central retinal vein occlusion with fluocinolone acetonide intravitreal implant 190 µg (ILUVIEN®)

52

LUCENTIS
RANIBIZUMAB INJECTION
EYLEA
aflibercept solution for injection

ANTI-VEGF

53

Etudes BRAVO et CRUISE


Ranibizumab for Macular Edema following Branch Retinal Vein Occlusion
Six-Month Primary End Point Results of a Phase III Study


Ranibizumab for Macular Edema following Central Retinal Vein Occlusion
Six-Month Primary End Point Results of a Phase III Study

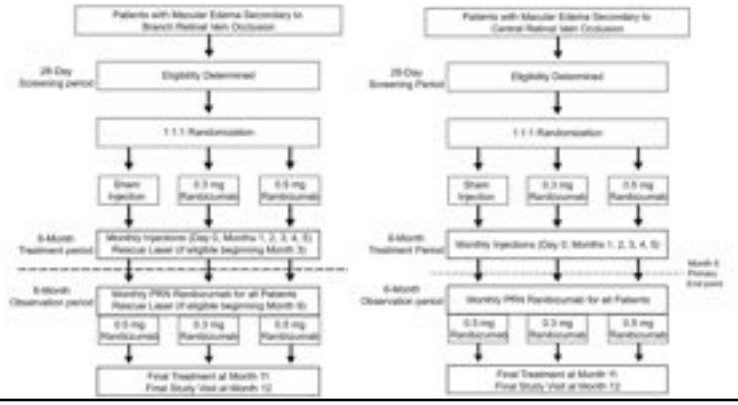
54

Patients inclus

- BRAVO
  - OBVR depuis < 12 mois
    Screening ≈ 1 mois
  - AV entre 20/400 et 20/40
  - Laser depuis > 4 mois
- CRUISE
  - OVCR depuis < 12 mois
    Screening ≈ 1 mois
  - AV entre 20/320 et 20/40
  - Laser depuis > 4 mois

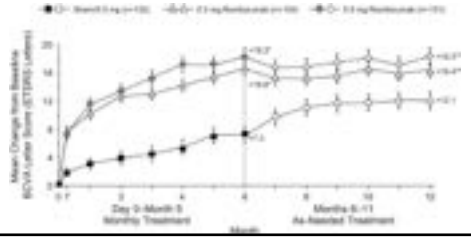
55

Design



56

Ranibizumab/OBVR : BRAVO

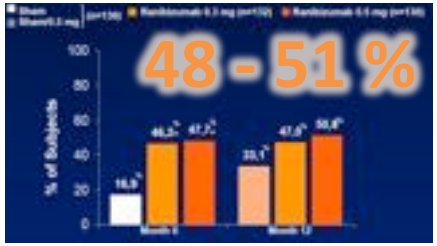


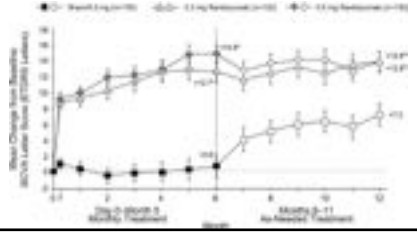
+18 lettres

Ophthalmology. 2011 Aug;118(8):1594–602

57

Ranibizumab/OVCR : CRUISE





+15 lettres (M6)
+14 lettres (M12)

Ophthalmology. 2011 Oct;118(10):2041–9

58

Tolérance générale

CRUISE	Sham	Lucentis
AVC hémorrag.	0	0
AVC ischémique	0	0
AIT	0	1 (0,8%)
IdM	1 (0,8%)	1 (0,8%)
Angor	0	1 (0,8%)
HTA	1 (0,8%)	0
Protéinurie	0	0

BRAVO	Sham	Lucentis
AVC hémorrag.	1 (0,8%)	1 (0,8%)
AVC ischémique	0	0
AIT		
IdM	0	1 (1,8%)
Angor	0	1 (1,8%)
HTA	0	0
Protéinurie	0	0

59

Tolérance oculaire

CRUISE	Sham	Lucentis
Inflammation	5 (3,9%)	2 (1,6%)
Cataracte	0	1 (0,8%)
Rubéose	9 (7%)	1 (0,8%)
GNV	2 (1,6%)	0
Endophtalmie	0	0
DR	0	0
Déchirure	0	0
HiV	1 (0,8%)	0

BRAVO	Sham	Lucentis
Inflammation	4 (3,1%)	0
Cataracte	4 (3,1%)	4 (3,1%)
Rubéose	3 (2,3%)	0
GNV	0	0
Endophtalmie	0	1 (0,8%)
DR	0	0
Déchirure	0	0
HiV	0	0

60

Tolérance oculaire

CRUISE	Sham	Lucentis
Inflammation	5 (3,9%)	2 (1,6%)
Cataracte	0	1 (0,8%)
Rubéose	9 (7%)	1 (0,8%)
GNV	2 (1,6%)	0
Endophtalmie	0	0
DR	0	0
Déchirure	0	
HiV		

BRAVO	Sham	Lucentis
Inflammation	4 (3,1%)	0
Cataracte	4 (3,1%)	
Rubéose		
GNV		
Endophtalmie		1 (0,8%)
DR		0
Déchirure	0	0
HiV	0	0

Injections mensuelles…

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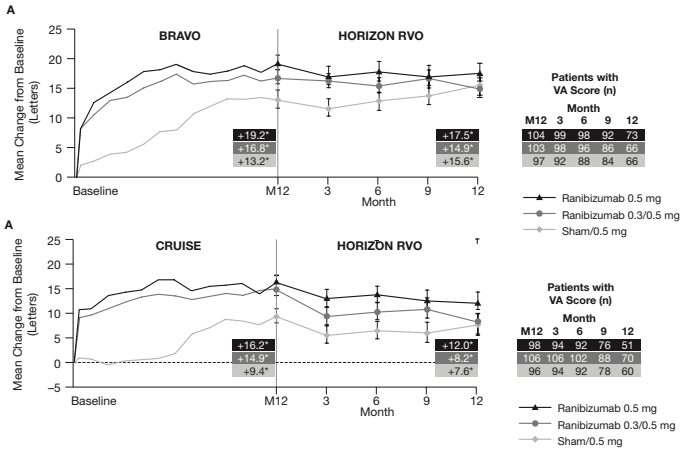
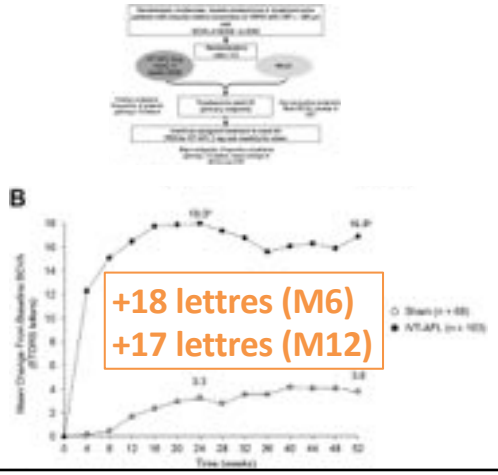
BRAVO/CRUISE au long cours : HORIZON

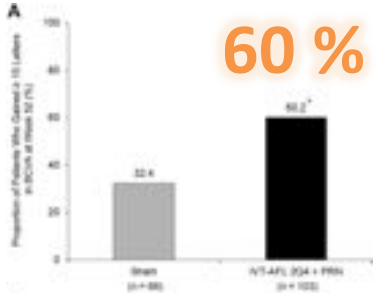


Ophthalmology. 2012 Apr;119(4):802–9

62

Aflibercept/OVCR : GALILEO



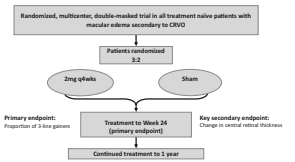


+18 lettres (M6)
+17 lettres (M12)

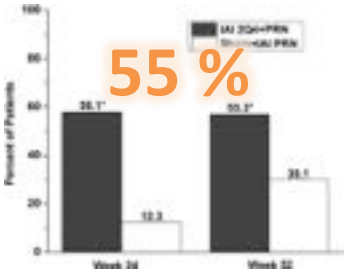
Ophthalmology. 2014 Jan;121(1):202–8

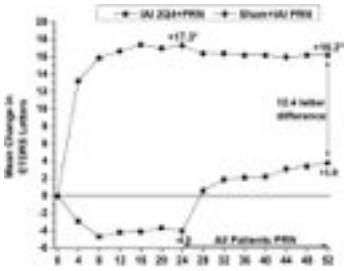
63

Aflibercept/OVCR : COPERNICUS



+17 lettres (M6)
+16 lettres (M12)





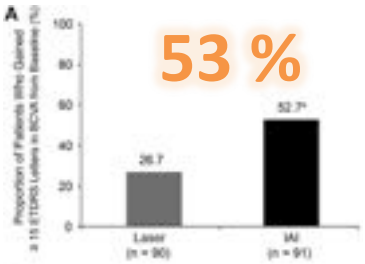
American Journal of Ophthalmology. 2013 Mar;155(3):429–37.e7

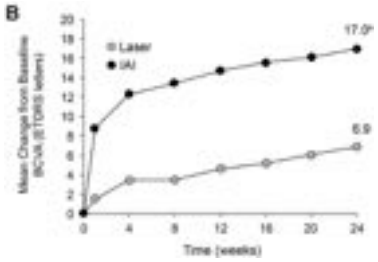
64

Aflibercept/OBVR : VIBRANT

+17 lettres (M6)

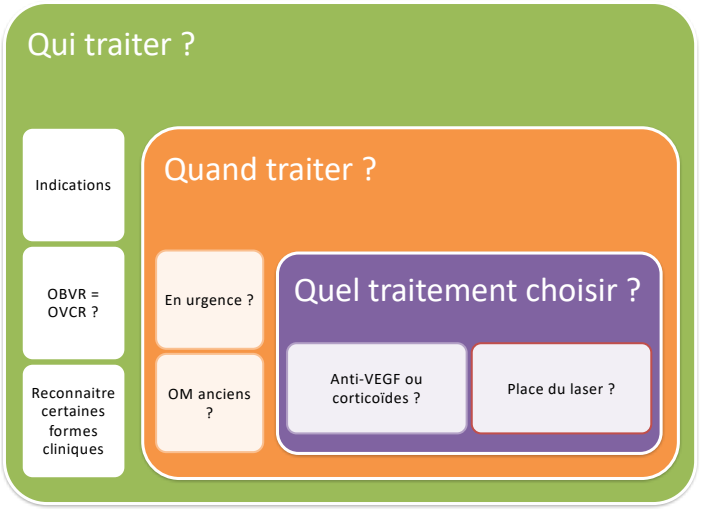
53 %





Ophthalmology [Internet]. 2014 Oct 11

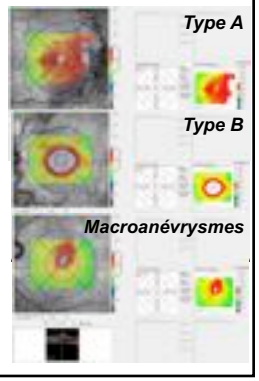
65



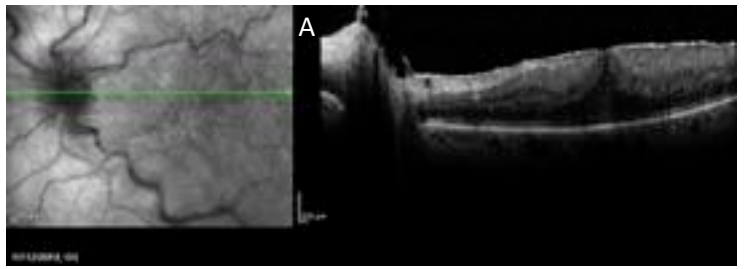
66

Tous les OM ne sont pas identiques

- OM central = rupture de la barrière hémato-rétinienne
- OM par extension d'un OP = type A
- OM décentré = rechercher TelCaps
- OM par MEM

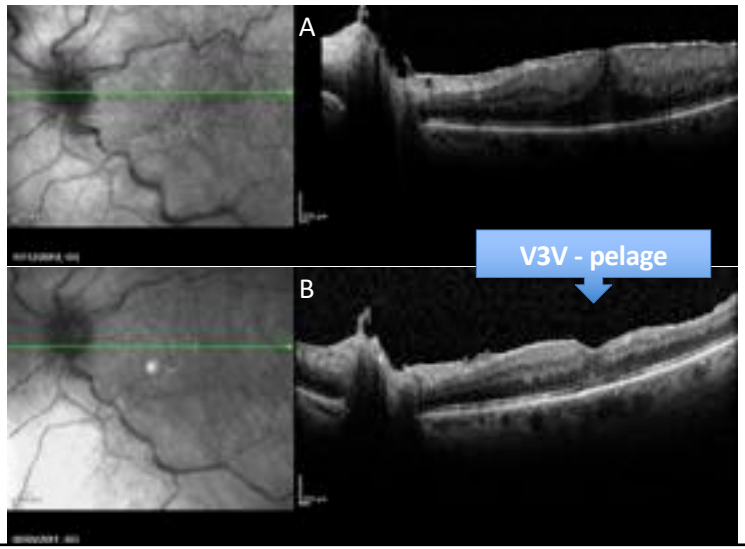


67



MEM ?

68



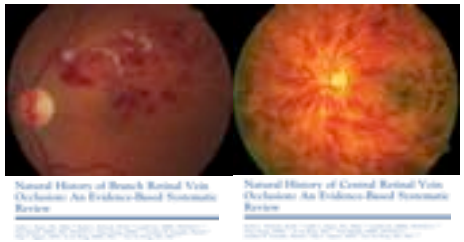
69

DISTINGUER CERTAINES FORMES CLINIQUES

70

OVCR ≠ OBVR

- Terrain
- Facteurs de risque
- Evolution
  - Guérison spontanée
  - Risque de GNV
- Hémi-occlusion ≈ OVCR
  - Moins de risque de GNV



- **40-50% de guérison** de l'OM
- Amélioration > BAV
- Gain > 2 lignes : 1/3 à ¾
- AV moyenne : +1 lettre (6m) à **+15 lettres** (18m) voire +28 lettres (12-24m)

- **30% de guérison** de l'OM
  - Mais *ischémie*
- AV moyenne
  - Ni : **- 3 lettres** (12m)
  - I : **-15** (6m) à -35 l. (12m)

CVOS :

- AV > 5/10 à 3 ans :
  - SI AVi > 5/10 : 65%
  - Si 1/10<AVi<5/10 : **20%**

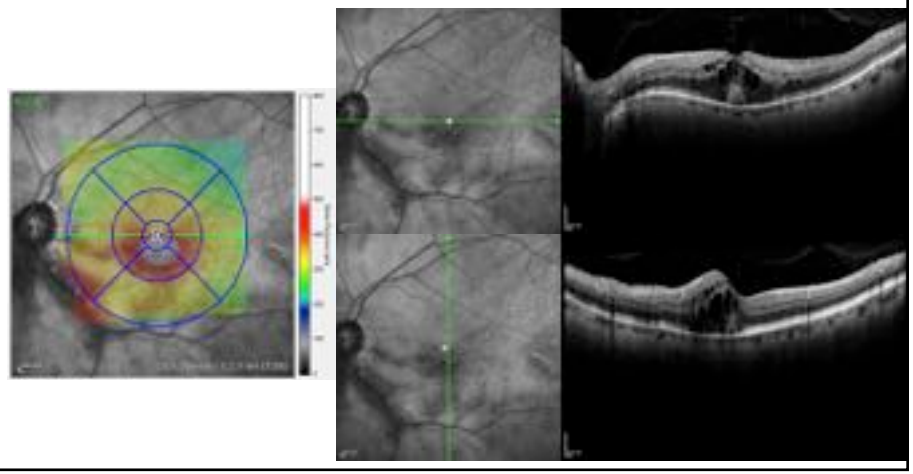
71

M. O, 71 ans

- Antécédents
  - HTA traitée
  - HTO sous monothérapie (latanoprost)
- Œil gauche : hémi-occlusion inférieure début novembre 2011
  - 4 novembre 2011
    - 5 à 6/10f TO=24
    - Surveillance
      - modification traitement (brimonidine + timolol)

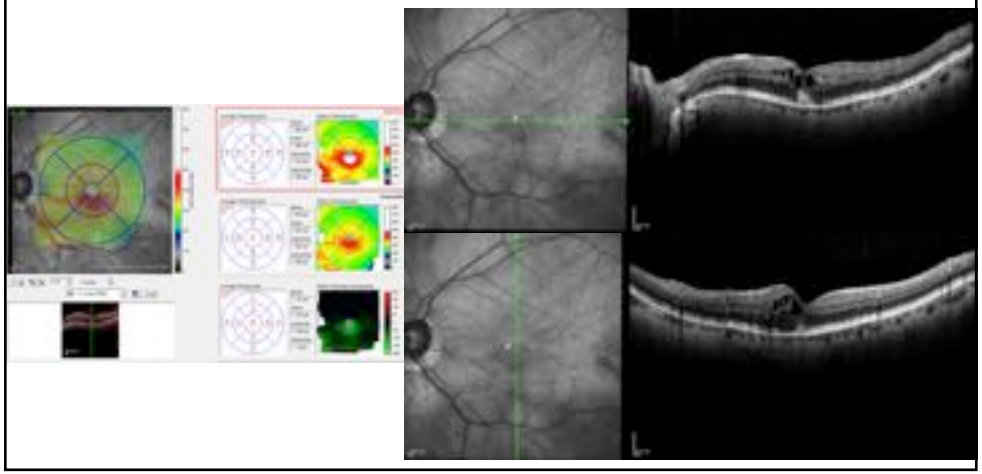
72

2 décembre 2011 (+1M) : 4/10, P2



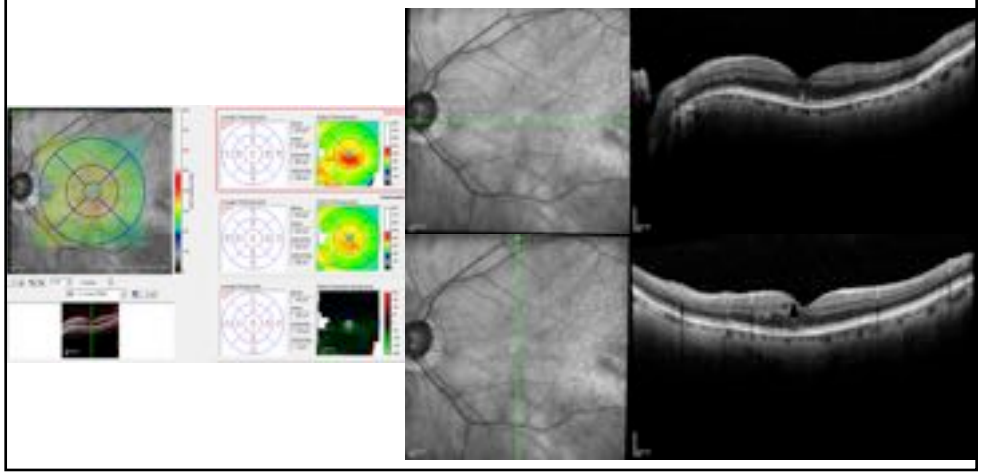
73

6 janvier 2012 (+2M) : 5/10f, P2



74

17 février 2012 (+3M) : 9/10, P2



75

Patchy Ischemic Retinal Whitening in Acute Central Retinal Vein Occlusion

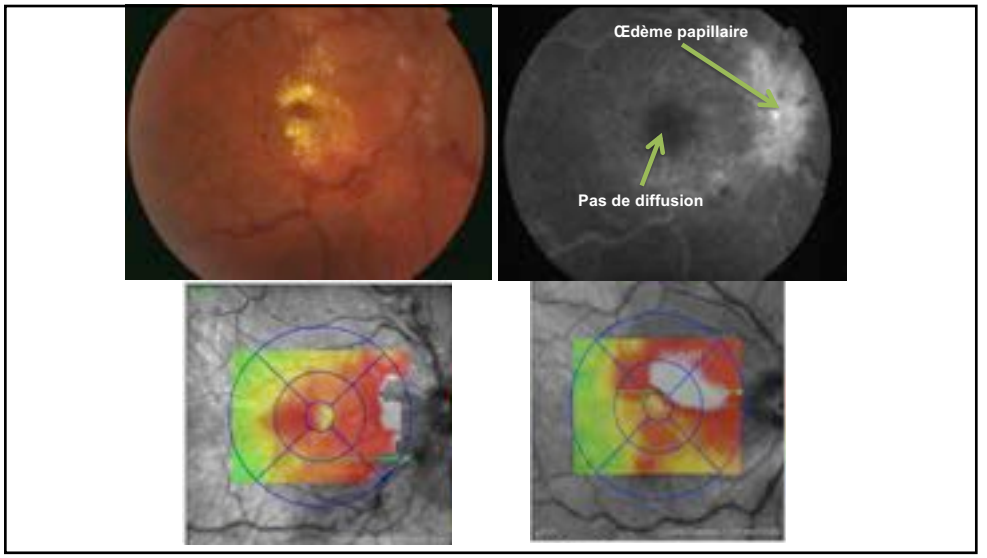
Perivascular Macular Whitening During Acute Central Retinal Vein Occlusion

BLANC PÉRI-VEINULAIRE (≈PAMM)

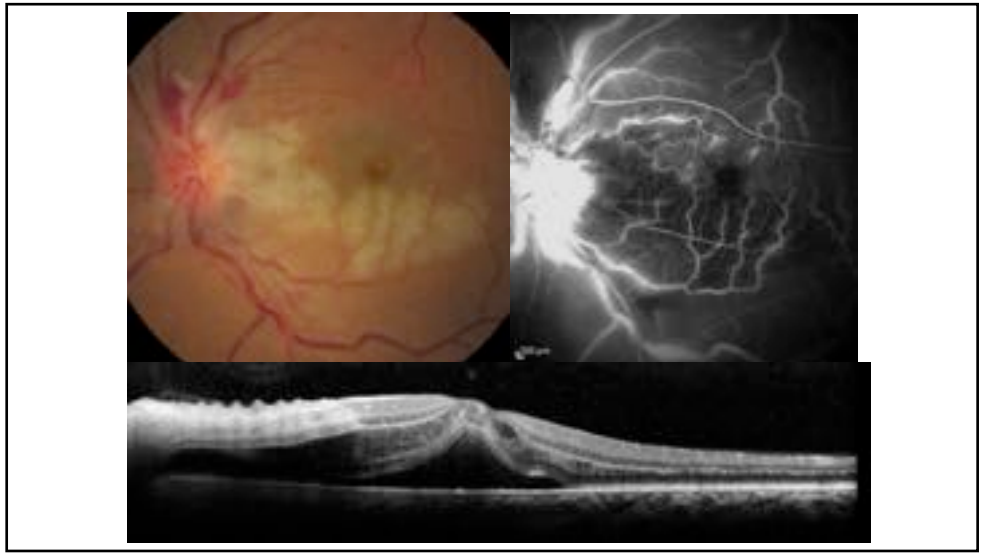
76


Patchy Ischemic Retinal Whitening in Acute Central Retinal Vein Occlusion

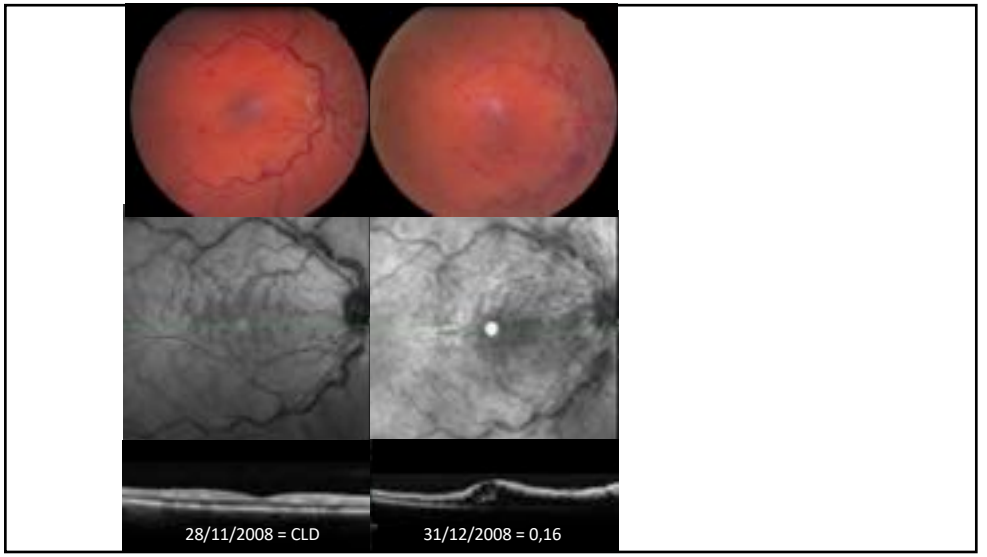
77


Œdème papillaire
Pas de diffusion

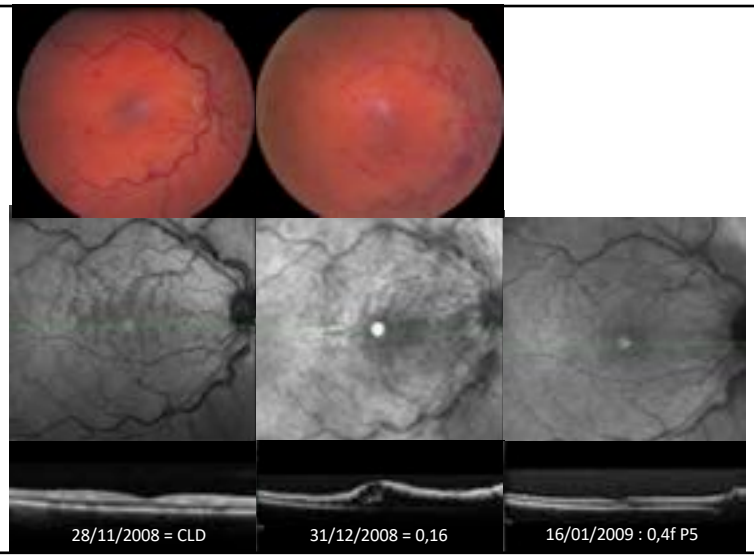
78



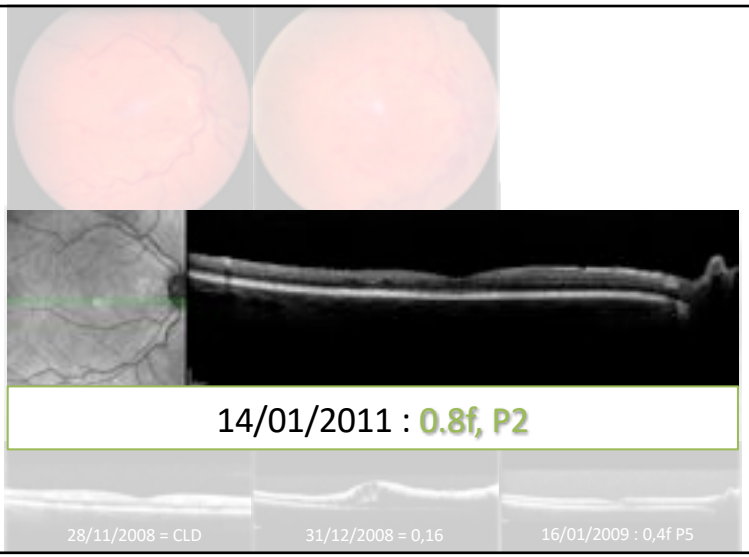
79


28/11/2008 = CLD
31/12/2008 = 0,16

80

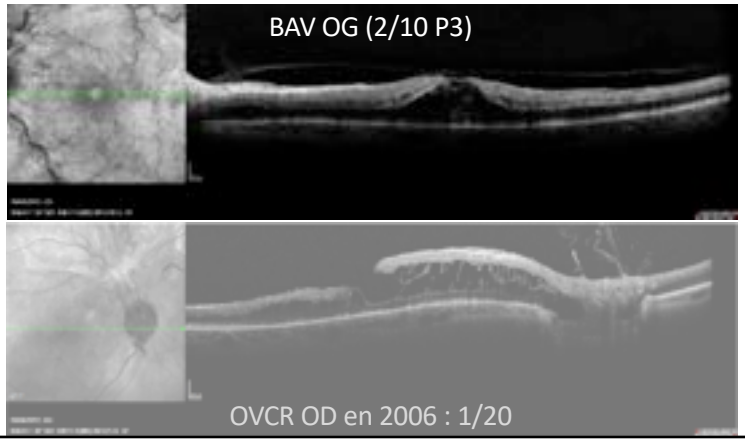


81



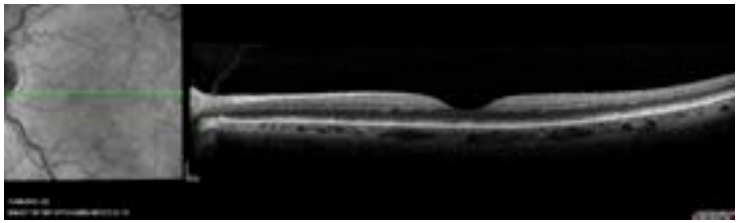
82

20 avril 2012



83

11 juin 2012



9/10, P2 !

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TRAITEMENT DE L'ŒDÈME MACULAIRE PAR RUPTURE DE LA BARRIERE HÉMATO-RÉTINIENNE

Critères d'inclusion des essais : AV

GENEVA
- 34 à 68 lettres ETDRS
- 20/200 à 20/50

CRUISE/BRAVO
- 20/400 (B) - 20/320 (C) à 20/40

GALILEO/COPERNICUS+VIBRANT
- 24 à 73 lettres ETDRS
- 20/320 à 20/40

BVOS
- AV < 5/10

Pas de donnée pour
AV > 4 – 5 /10
< 1/16 – 1/20

Acuité visuelle moyenne

GENEVA

Mean baseline visual acuity, letters ± SD (Snellen equivalent)	54.3±9.93 (20/80)	53.9±10.41 (20/80)	54.8±9.86 (20/80)

BRAVO

BCVA			
ETDRS letter score			
Mean (SD)	54.7 (12.2)	56.0 (12.1)	53.0 (12.5)
Range	16–73	25–73	22–79
Distribution, n (%)			
<34	9 (6.8)	9 (6.7)	13 (9.9)
35–54	50 (37.9)	48 (35.8)	49 (37.4)
≥55	73 (55.3)	77 (57.5)	69 (52.7)
Approximate Snellen equivalent, median	20/80	20/63–20/80	20/80

CRUISE

BCVA			
ETDRS letter score			
Mean (SD)	49.2 (14.7)	47.4 (14.8)	48.1 (14.6)
Range	16–71	9–72	21–73
Distribution, n (%)	—	—	—
<34	26 (20.0)	33 (25.0)	30 (23.1)
35–54	49 (37.7)	46 (34.8)	50 (38.5)
≥55	55 (42.3)	53 (40.2)	50 (38.5)
Approximate Snellen equivalent, median	20/100	20/100	20/100

VIBRANT

BCVA		
Mean, letters (SD)	57.7 (11.3)	58.6 (11.4)
>20/200 (35–73 letters), n (%)	83 (92.2)	85 (93.4)
≤20/200 (24–34 letters), n (%)	7 (7.8)	6 (6.6)

COPERNICUS GALILEO

BCVA >20/200, n(%)	55 (75.3%)	86 (75.4%)	141 (75.4%)
BCVA ≤20/200, n(%)	18 (24.7%)	28 (24.6%)	46 (24.6%)
Mean central retinal thickness (SD), µm	672.4 (245.3)	661.7 (237.4)	665.8 (239.8)
Mean visual acuity (ETDRS)	48.9 (14.4)	50.7 (13.9)	50.0 (14.1)
Mean ETDRS BCVA letter score (SD)	53.6 (15.8)	50.9 (15.4)	52.2 (15.7)
ETDRS BCVA >20/200	86 (83.5%)	56 (82.4%)	142 (83.0%)

2 à 2,5/10

Selon l'OCT ?

- Mauvaise corrélation épaisseur - AV
  - Si épaisseur centrale > 700µ : espoir d'AV finale ≥5/10 est quasi-nulle

… Mais on ne traite pas un OCT !

Martinet V & al. ARVO 2008

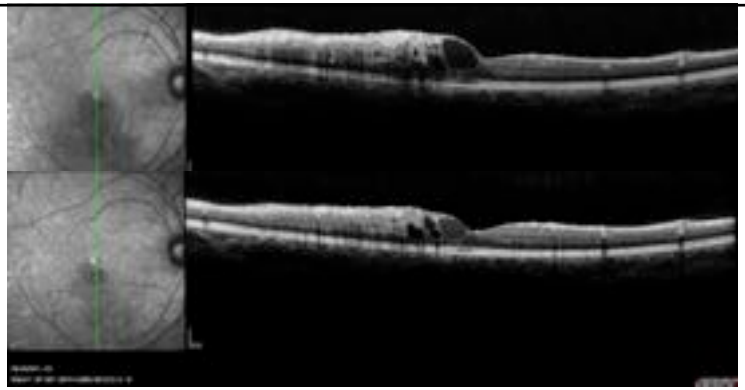
- 1 avril 2011
  - BAV depuis 1 mois
  - 4/10f

89

- 1 avril 2011
  - BAV depuis 1 mois
  - 4/10f

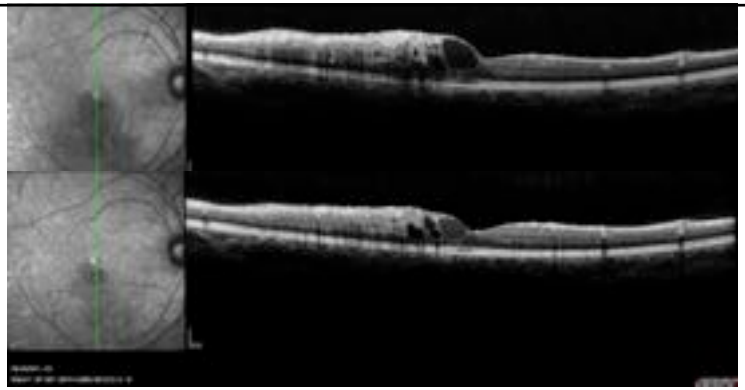
➔ Surveillance (2 mois)

90



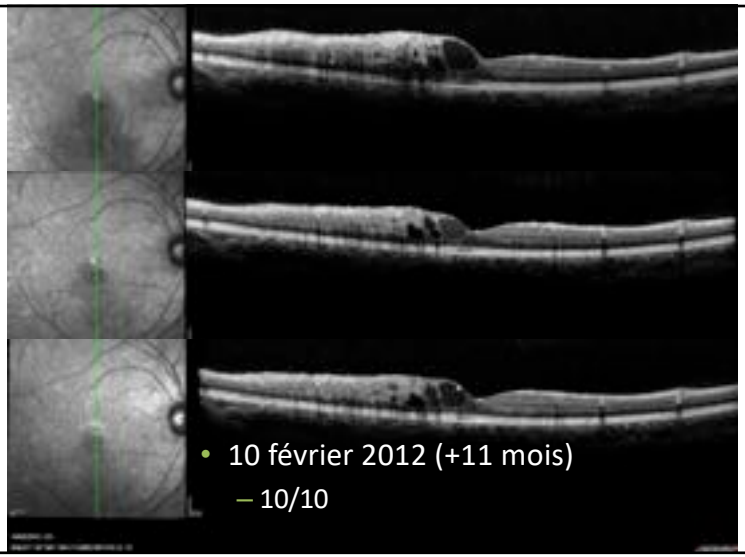
- 28 octobre 2011 (+7-8 mois)

91



- 28 octobre 2011 (+7-8 mois)
  - 12/10, P2 !

92



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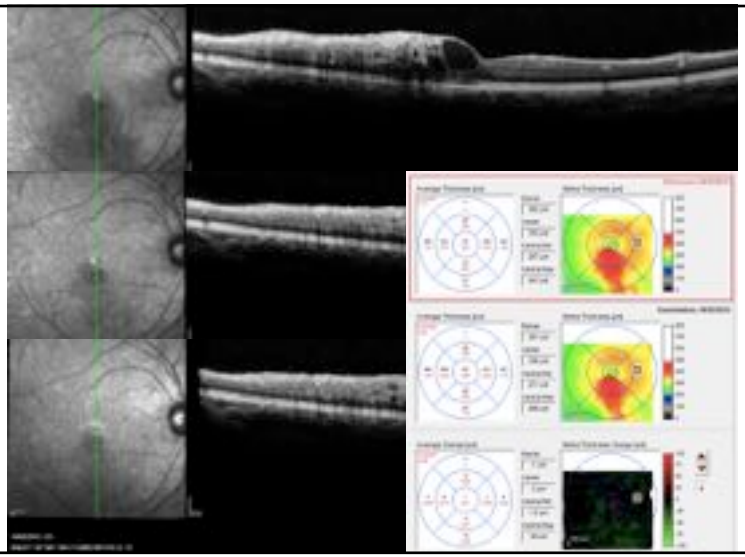

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Selon non-perfusion / ischémie ?

- Critère de non-inclusion dans certains essais…
  - GENEVA, CRUISE
- Contre-indication (relative) ?
  - RCP

Ozurdex n'a pas été étudié chez les patients souffrant d'un œdème maculaire consécutif à une occlusion de la veine rétinienne avec ischémie rétinienne significative. De ce fait, Ozurdex n'est donc pas recommandé chez ces patients.

Antécédents d'OVR, forme ischémique d'OBVR ou d'OVCR :
Les données concernant le traitement des patients ayant des antécédents d'OVR et des patients présentant une forme ischémique d'occlusion de branche veineuse rétinienne (OBVR) ou d'occlusion de la veine centrale de la rétine (OVCR) sont limitées. Le traitement n'est pas recommandé chez les patients présentant une OVR associée à des signes cliniques d'ischémie ayant entraîné une perte irréversible de la vision.

  - HAS (Commission de transparence)

Une angiographie à la fluorescéine doit être réalisée avant la mise sous traitement afin d'écarter les formes ischémiques qui ne sont pas des indications de LUCENTIS. L'évolution de la forme œdémateuse vers la forme ischémique est possible sous traitement et il est recommandé de la surveiller.

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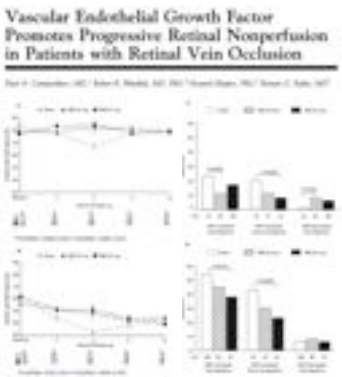
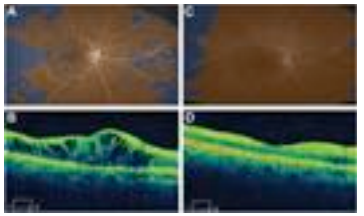
Anti-VEGF et non-perfusion



Vascular Endothelial Growth Factor Promotes Progressive Retinal Nonperfusion in Patients with Retinal Vein Occlusion

Ophthalmology. 2013 Apr;120(4):795–802



AREA OF PERIPHERAL RETINAL NONPERFUSION AND TREATMENT RESPONSE IN BRANCH AND CENTRAL RETINAL VEIN OCCLUSION

MICHAEL SINGER, MD,* COLIN S. TAN, FRCSEd (Ortho),†‡§ DARREN BELL, MD,* SRINIVAS R. SADDA, MD§

Retina. 2014 Sep;34(9):1736-42

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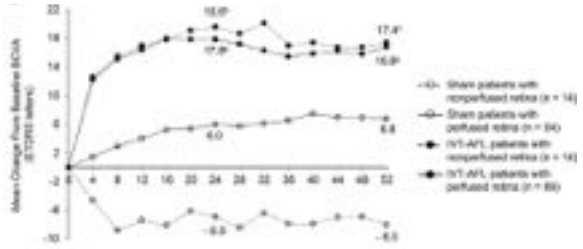
Selon non-perfusion / ischémie ?

- Critère de non-inclusion dans certains essais
  - GENEVA, CRUISE
- Contre-indication (relative) ?
- GALILEO/COPERNICUS : ≈ 10-15% non perfusées



Ophthalmology. 2014 Jan;121(1):202–8

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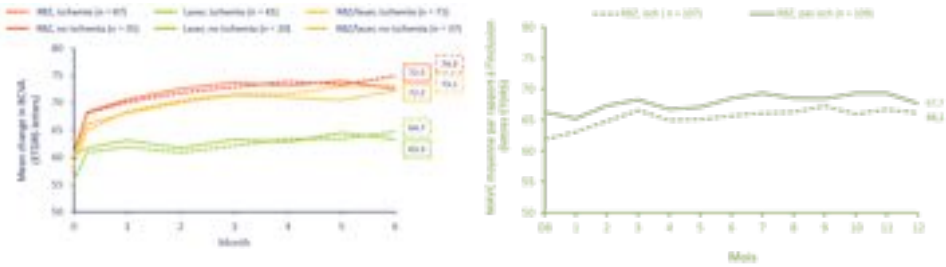
BRIGHTER / CRYSTAL



98

Au total,

- Ne pas traiter toutes les OVR,
  - ni tous les OM/OCT
- Mais un patient avec BAV
  - Peu d'argument pour traiter si
    - AV supérieure à 5-6/10
    - AV inférieure à 1/20
  - A moduler selon
    - Plainte fonctionnelle
    - Mode de vie, activités, exigences…
- Patient vs. moyennes
  - Information et balance bénéfice/risque individuelle

99

QUAND TRAITER ?

100

« 3 mois » ?

- Depuis la « BVOS »

L'arrivée des nouveaux traitements /IVT change-t-elle la donne ?

- **Traiter plus tôt ?**
  - Fait plaisir à l'industrie pharmaceutique
  - Taux de guérison spontané non négligeable
  - Expose à des traitements inutiles
  - Formes cliniques particulières
- **Est-il utile de proposer le traitement « tard » ?**

Essais cliniques Ph.III : durée moyenne d'évolution

GENEVA : ≈ 5 mois

Duration of macular edema			
Mean duration (range)	157.6 (19–374)	153.0 (49–944)	156.1 (19–374)

BRAVO : ≈ 3 ½ mois

Months from RVO diagnosis to screening	
Mean (SD)	
Median	
Range	

CRUISE : ≈ 3 à 3 ½ mois

Months from RVO diagnosis to screening	
Mean (SD)	2.
Median	
Range	(

GALILEO : ≈ 2 ½ à 3 mois

Mean time since CRVO diagnosis in days (SD)	78.0 (89.6)

COPERNICUS : ≈ 2 à 2 ½ mois

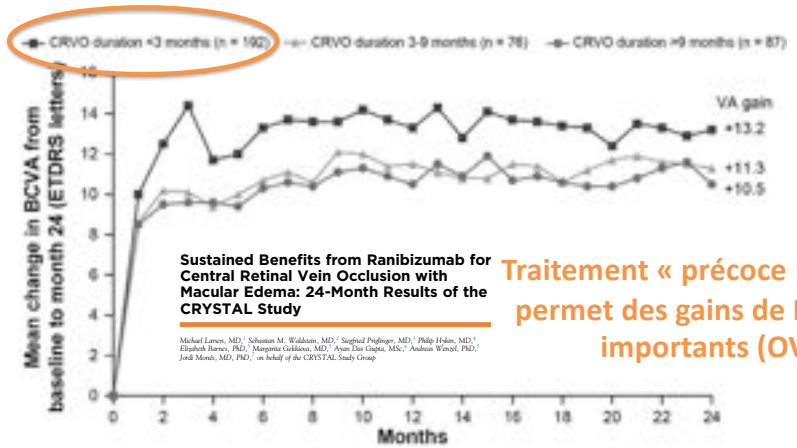
Mean time since CRVO diagnosis (mos)	1.88 (2.19

VIBRANT : ≈ 1 ½ mois

Time since BRVO diagnosis Mean, days (SD)		
	43.1 (38.8)	42.4 (43.4)

Pas/Peu de données sur l'intérêt de débuter les injections avant 1 – 1,5 mois d'évolution

CRYSTAL : gain AV selon le délai



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

Michael Larsen, MD,[1] Sebastian M. Waldstein, MD,[2] Siegfried Priglinger, MD,[3] Philip Hykin, MD,[4] Elizabeth Barnes, PhD,[5] Margarita Gekkieva, MD,[5] Ayan Das Gupta, MSc,[6] Andreas Wenzel, PhD,[5] Jordi Monés, MD, PhD,[7] on behalf of the CRYSTAL Study Group

Traitement « précoce » (< 3 mois) permet des gains de MAVC plus importants (OVCR)

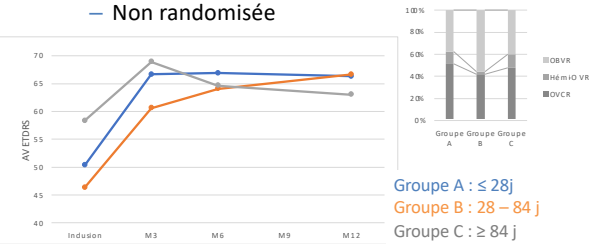
Ophthalmology Retina 2018;2:134–42

Influence du délai de traitement

Impact of Time to Anti-Vascular Endothelial Growth Factor Intervention on Visual Outcomes for Patients Diagnosed With Retinal Vein Occlusion

Jessica Hsueh, BS; Karen M. Wai, MD; Felipe F. Conti, MD; Thais F. Conti, MD; Rishi P. Singh, MD

– Non randomisée



Groupe A : ≤ 28j
Groupe B : 28 – 84 j
Groupe C : ≥ 84 j

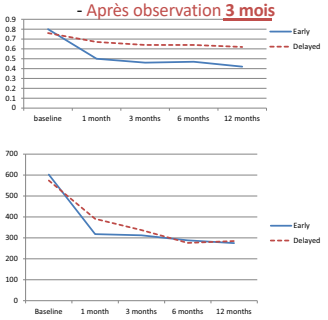
– Moindre récupération si délai « long » > 3 mois…
  - GrC : 346 jours en moyenne !

Ophthalmic Surg Lasers and Imaging Retina 2018;49:832–7

Comparison of immediate versus deferred intravitreal Bevacizumab in macular oedema due to branch retinal vein occlusion: a pilot study

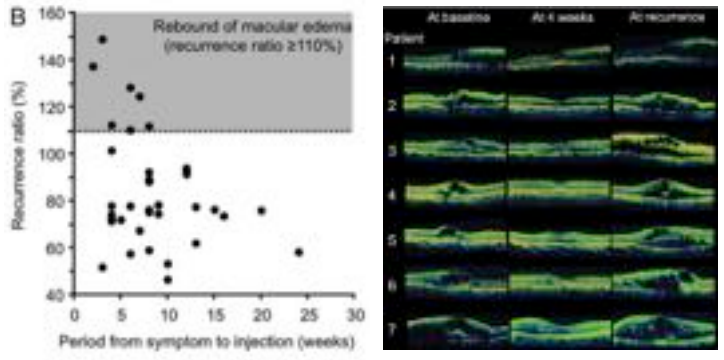
M. A. Khan · Varakutti Mallika · Duttakiran Joshi

OVR < 1 mois, randomisation :
- Traitement immédiat
- Après observation 3 mois



Int Ophthalmol. 2018;38:943–9

REBOUND OF MACULAR EDEMA AFTER INTRAVITREAL BEVACIZUMAB THERAPY IN EYES WITH MACULAR EDEMA SECONDARY TO BRANCH RETINAL VEIN OCCLUSION



Retina. 2011;31(6):1075–82.

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Donc…

Pas/Peu de données sur
l'intérêt de débuter un traitement
avant 1 – 1,5 mois d'évolution…

Moindre gain d'acuité visuelle
lorsque le traitement est
différé de **plus de 3 mois.**

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Intérêt de débuter un traitement tardivement ?

- Groupes « témoins » des études de phase 3 traités à 6 mois si besoin

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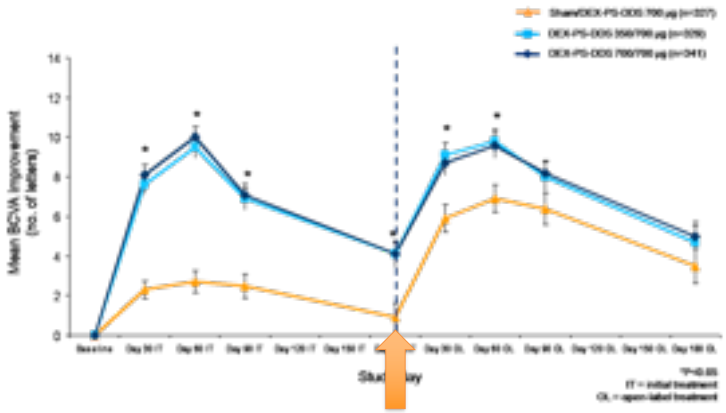
GENEVA : Réinjection corticoïde (700µg)



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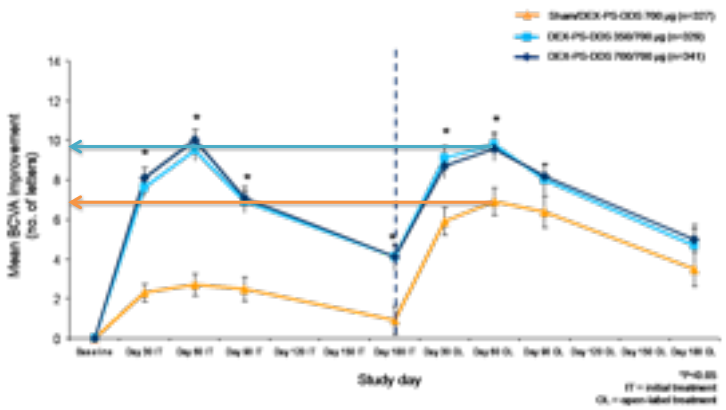
GENEVA : Réinjection corticoïde (700µg)



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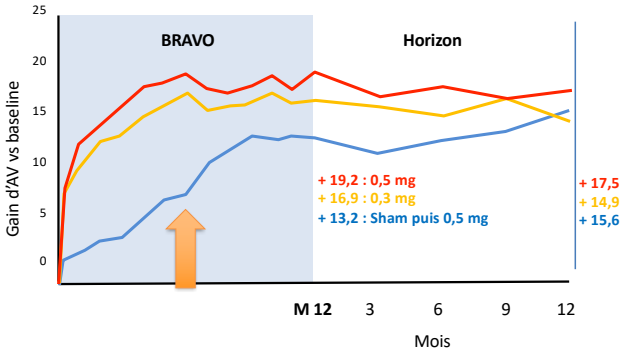
Suivi des patients de BRAVO



PA Campochiaro , ARVO 2011, Poster 4869

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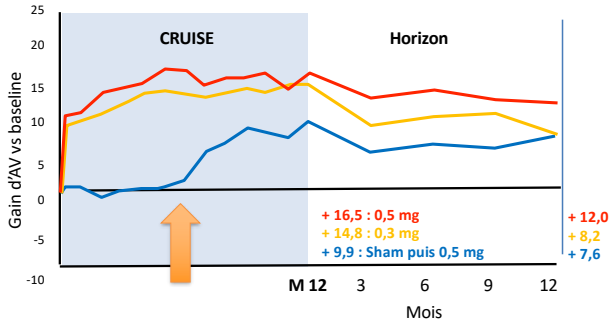
Suivi des patients de CRUISE



- **Tolérance : pas de nouvel évènement**
  - 2 à 9% d'EI oculaires sévères (2 endophtalmies chez patients de CRUISE)
  - 1 à 6% d'EI systémiques sévères potentiellement liés à l'inhibition du VEGF

PA Campochiaro , ARVO 2011, Poster 4869

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Modalités de poursuite du traitement

- Réinjection(s) à la demande
  - 38 à 40% : 1 seule injection
  - Moyenne : 2,6 à 2,8 injections

Outcome of "treat and monitor" regimen of aflibercept and ranibizumab in macular edema secondary to non-ischemic branch retinal vein occlusion

Francesco Pichi · Ahmed Mohammed Elbarky · Tarek Roshdy Elhamaky

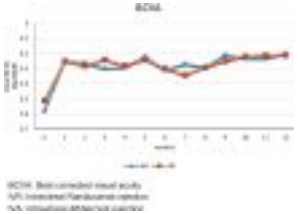
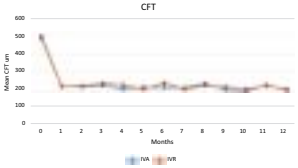


Fig. 2 Best corrected visual acuity change over 12 months in the ranibizumab (0.31 ± 0.1 logMAR) and aflibercept (0.38 ± 0.15 logMAR) "treat and observe" groups



Int Ophthalmology 2019;39:145–53

112

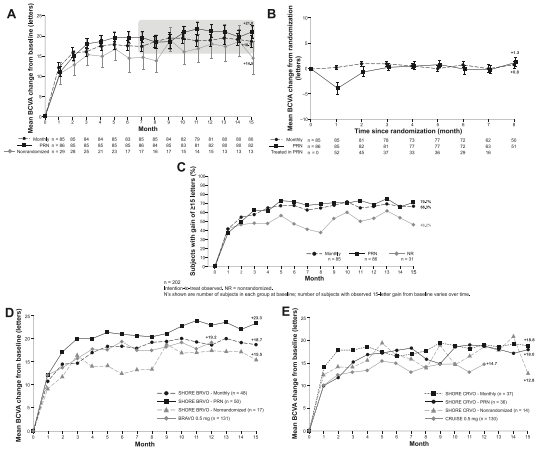
PRN vs mensuel

- AMM (anti-VEGF) : réinjections jusqu'à stabilité
- Puis reprise si BAV

Monthly Versus As-Needed Ranibizumab Injections in Patients with Retinal Vein Occlusion

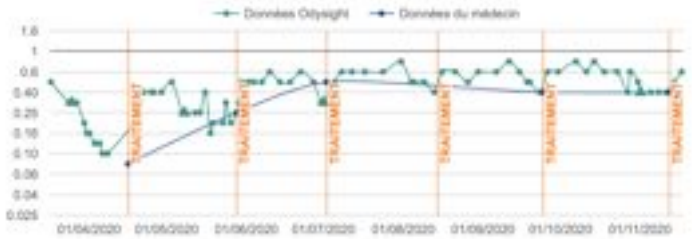
The SHORE Study

Peter A. Campochiaro, MD,[1] Charles C. Wykoff, MD, PhD,[2] Michael Singer, MD,[1] Robert Johnson, MD,[3] Dennis Marcus, MD,[3] Linda Yau, PhD,[4] Gary Sternberg, MD, MBA[4]



Ophthalmology 2014;121(12):2432-2442. doi:10.1016/j.ophtha.2014.06.011

Intérêt d'applications de suivi à domicile ?



Treat & Extend, si récidives fréquentes

JAMA Ophthalmology | Original Investigation

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, MD, MPH; Paul C. VanVeldhuisen, PhD; Michael S. Ip, MD; Barbara A. Blodi, MD; Neal L. Oden, PhD; Michael Altaweel, MD; Daniel M. Bernstein, MD; for the SCORE2 Investigator Group

Figure 1. Mean Visual Acuity Letter Score Over Time

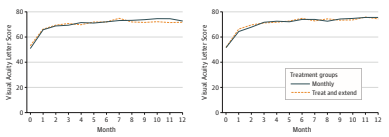
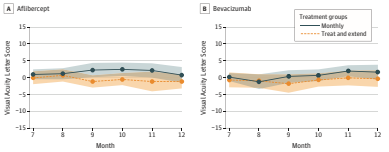


Figure 2. Visual Acuity Letter Score Mean Change in Months 7 Through 12



eTable 2: Description of Anti-VEGF Treatments between Months 6 and before Month 12 Visit

	Aflibercept		Bevacizumab	
	Monthly (N=79)	Treat and Extend (N=80)	Monthly (N=67)	Treat and Extend (N=67)
Anti-VEGF Injections				
Mean* (SD)	5.8 (0.7)	3.8 (1.2)	5.8 (0.7)	4.5 (1.2)
	P<0.001		P<0.001	
Min, Median, Max	2, 6, 6	1, 3, 6	3, 6, 6	1, 5, 6
Average days between injections within participants*				
Mean days (SD)	29.6 (4.3)	46.8 (18.4)	29.4 (5.0)	39.6 (8.6)
	P<0.001		P<0.001	
Longest extension between injections for TAE schedule within participant				
4-weeks	NA	11 (13.8%)	NA	20 (29.9%)
6-weeks		14 (17.5%)		17 (25.4%)
8-weeks		45 (56.3%)		24 (35.8%)
10-weeks		10 (12.5%)		6 (9.0%)
	P=0.03** comparing Aflibercept TAE to Bevacizumab TAE (chi-square 3 df test)			
TAE patterns				
Never extending	NA	11 (13.8%)	NA	20 (29.9%)
Always extending		45 (56.3%)		21 (31.3%)
Some extending, but also re-set back to 4-week intervals		24 (30.0%)		26 (38.8%)
	P=0.006** comparing Aflibercept TAE to Bevacizumab TAE (chi-square 2 df test)			
Total number of injections	454	303	387	304
Percent of injections within +/- 7 days of injection date target	91%	96%	93%	95%

JAMA Ophthalmol 2018;136(4):337. doi:10.1001/jamaophthalmol.2017.6843

Jusqu'à quand ?

Long-term Outcomes in Patients with Retinal Vein Occlusion Treated with Ranibizumab

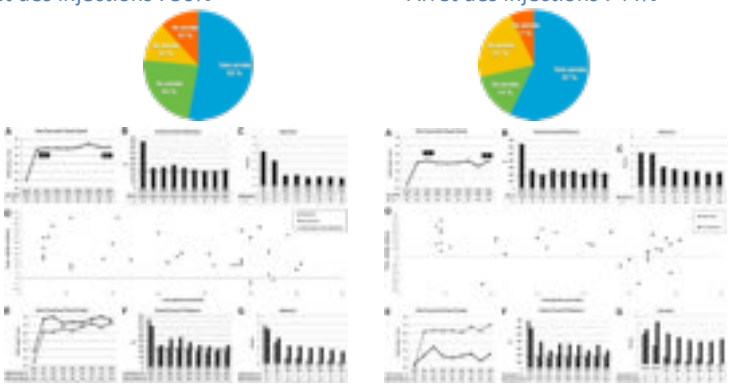
The RETAIN Study

OBVR

- Arrêt des injections : 50%

OVCR

- Arrêt des injections : 44%



Campochiaro PA & al. Ophthalmology. 2014 Jan;121(1):209–19

Jusqu'à quand ?

Long-term Outcomes in Patients with Retinal Vein Occlusion Treated with Ranibizumab
The RETAIN Study

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OVCR

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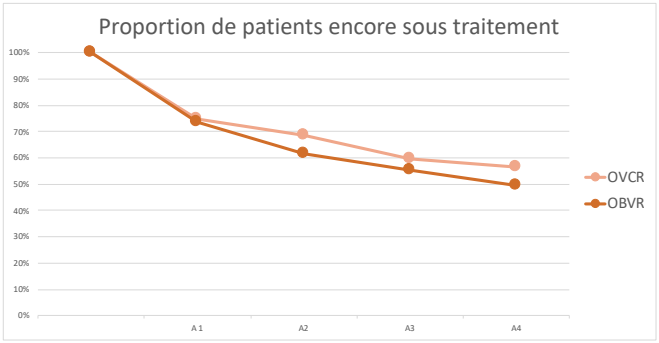


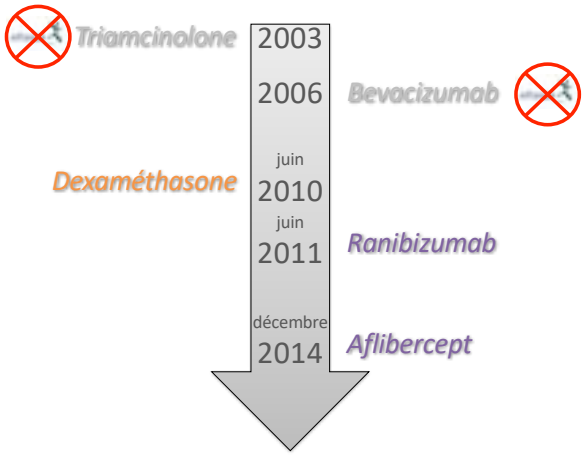
117

Injections intra-vitréennes

CHOIX ET MODALITÉS DU TRAITEMENT

118

Médicaments utilisés



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Comparaison anti-VEGF / corticoïdes

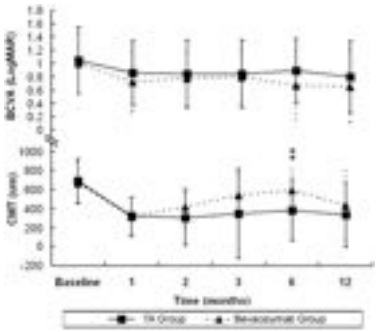
Intravitreal bevacizumab vs triamcinolone acetonide for macular oedema due to central retinal vein occlusion

CLINICAL STUDY

- 72 OVCR, délai 6 à 7 mois :
  - Triamcinolone 4mg : 42
  - Bevacizumab : 30
- Suivi > 3mois (7.8 ±4.3)

120

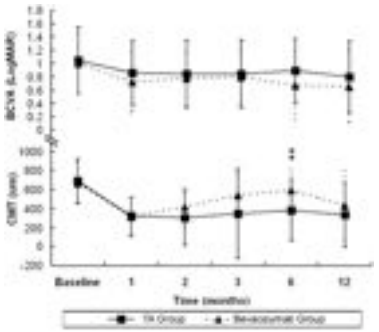
Efficacité



NB : pas de chirurgie cataracte

121

Nombre injections



- Triam. : 1 à 2
  - 1.3 ±0.4
- Beva. : 1 à 6
  - 2.7 ±1.8

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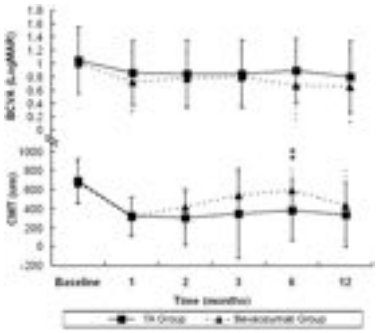
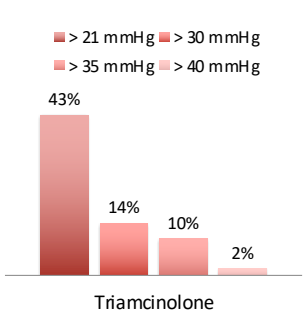
HTO





Bevacizumab : pas de variation TO

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Intravitreal dexamethasone implant versus anti-VEGF injection for treatment-naïve patients with retinal vein occlusion and macular edema: a 12-month follow-up study

C. Chiquet · C. Dupuy · A. M. Bron · F. Aptel · M. Straub · R. Isaico · J. P. Romanet · C. Creuzot-Garcher

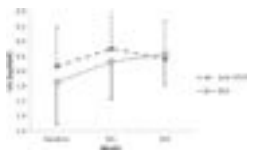

Fig. 1 Visual acuity at 1-month (M1) and 3-month (M3) visits for the 102 treatment-naïve patients. There was no significant difference in mean BCVA values at baseline ($p=0.06$), M1 ($p=0.06$), or M3 ($p=0.5$) between the anti-VEGF and DEX groups.

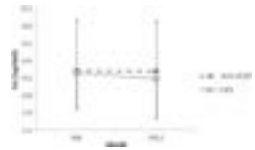

Fig. 2 Visual acuity at the 6-month (M6) and 12-month (M12) visits for the 77 treatment-naïve patients. No significant difference in mean BCVA values were noted between the two groups at M6 ($p=0.1$) or M12 ($p=0.2$).

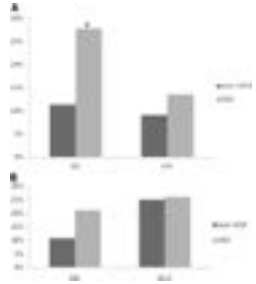

Fig. 5 **a** Good-responder rate at 1-month (M1) and 3-month (M3) visits for the 102 treatment-naïve patients. The number of "good responders" was significantly lower in the anti-VEGF group than in the DEX group at M1 ($p=0.04$). There was no significant difference between the two groups at M3. **b** Good-responder rate at 6-month (M6) and 12-month (M12) visits for the 77 treatment-naïve patients. There was no significant difference between the two groups at M6 or M12.

Graefes Arch Clin Exp Ophthalmol. 2015 Dec;253(12):2095-102. Epub 2015 Feb 12

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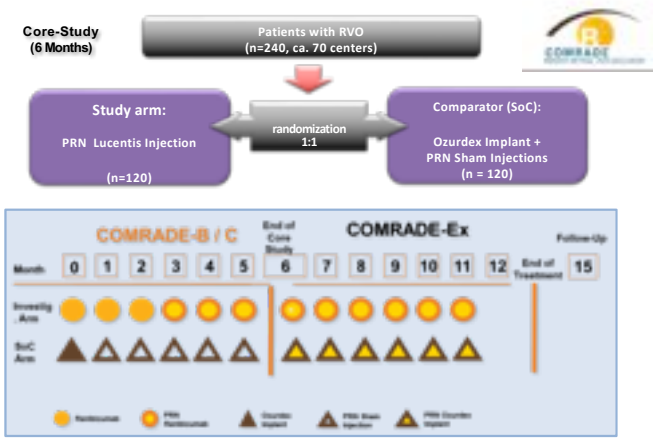
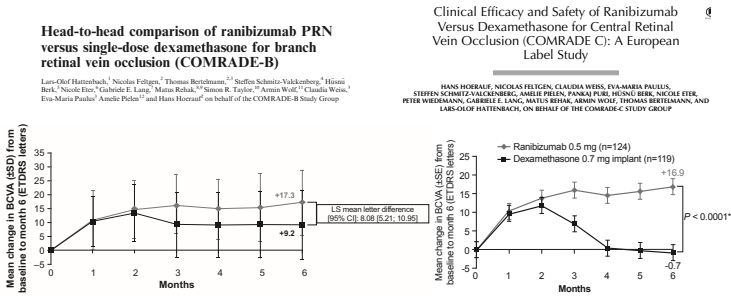
COMRADE



125

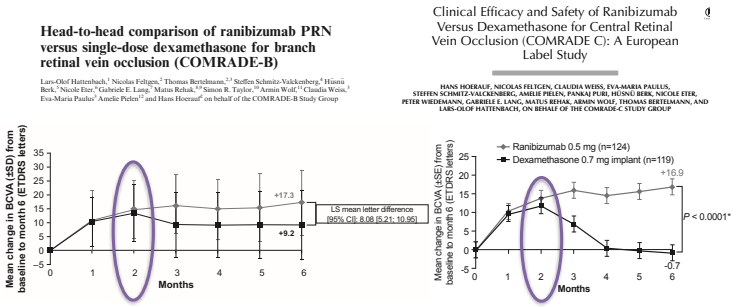
Ozurdex semble moins efficace que les anti-VEGF



… si l'on respecte l'AMM (pas de réinjection avant 6 mois)

126

Ozurdex est aussi efficace à 2 mois



127

COMRADE : hypertonie

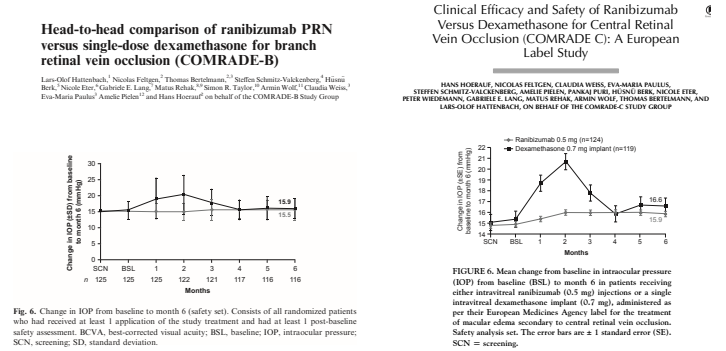


Fig. 6. Change in IOP from baseline to month 6 (safety set). Consists of all randomized patients who had received at least 1 application of the study treatment and had at least 1 post-baseline safety assessment. BCVA, best-corrected visual acuity; BSL, baseline; IOP, intraocular pressure; SCN, screening; SD, standard deviation.

FIGURE 6. Mean change from baseline in intraocular pressure (IOP) from baseline (BSL) to month 6 in patients receiving either intravitreal ranibizumab (0.5 mg) injections or a single intravitreal dexamethasone implant (0.7 mg), administered as per their European Medicines Agency label for the treatment of macular edema secondary to central retinal vein occlusion. Safety analysis set. The error bars are ± 1 standard error (SE). SCN = screening.

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	Anti-VEGF	Corticoïdes
OVCR récente	Protège du GNV	Vasoconstricteur
Ischémie étendue		
Patient phake, jeune		Risque de cataracte précoce
Antécédent HTO/GCAO	HTO au long cours ? **Pics ?**	HTO cortico-induite
AVC récent	Patients exclus des essais de phase III	Pharmacocinétique inchangée
Œil vitrectomisé	Demi-vie raccourcie ?	
Aphake / ICA		Risque de passage en CA
Disponibilité, récidives fréquentes	Cs ± Injections mensuelles	Injections tous les 4 à 6 mois (⚠ surveillance)
Au total :	En première intention en cas d'OVCR récente et/ou risque de GNV	En cas de récidives fréquentes et/ou en première intention si absence de risque de GNV (notamment OBVR)

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Anti-VEGF le plus souvent en 1ère intention

A préférer si :

- risque de GNV
  - Notamment OVCR
    - ce d'autant qu'elle est récente
  - non-perfusion étendue
- patient jeune phake
  - Aphake/ICA
- hypertonie/glaucome

A éviter si :

- antécédent de vitrectomie
- impossibilité de consultation/injection mensuelle.

130

Corticoïdes

A éviter si :

- Hypertonie / glaucome
- patient jeune et phake
  - risque de cataracte précoce, unilatérale
- Aphake
- d'une manière générale : OVCR récentes
  - risque de GNV

Préférés si :

- antécédent de vitrectomie
- récidives fréquentes
  - injections d'anti-VEGF répétées
- absence de risque de GNV
  - notamment OBVR

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Choix du traitement

REVUE GÉNÉRALE

Occlusions veineuses rétiniennes☆

Retinal vein occlusions

A. Pierru*, J.-F. Girmens, E. Héron, M. Paques

Centre national d'ophtalmologie des Quinze-Vingts, 28, rue de Charenton, 75012 Paris, France

Reçu le 21 février 2017 ; accepté le 3 avril 2017

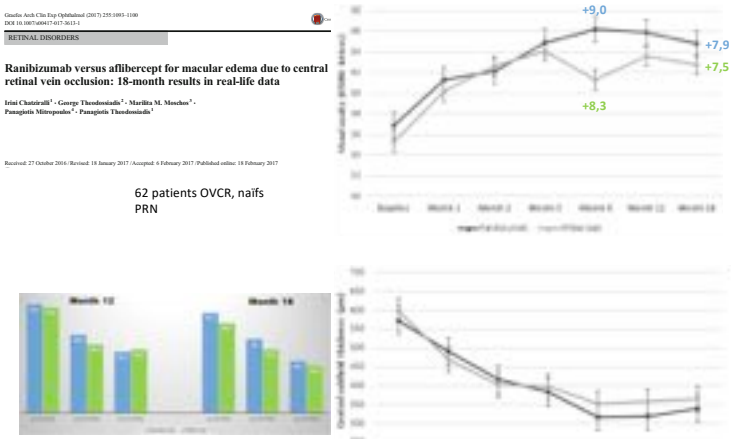
Il n'existe pas de consensus concernant la rapidité de mise en œuvre du traitement de l'œdème maculaire post OVCR ni du choix du traitement. Cependant, leur meilleure sécurité d'emploi, et leurs propriétés antiangiogéniques rendent les anti-VEGF plus séduisants comme traitement des formes récentes.

J Fr Ophtalmol 2017;40:696–705

132

133

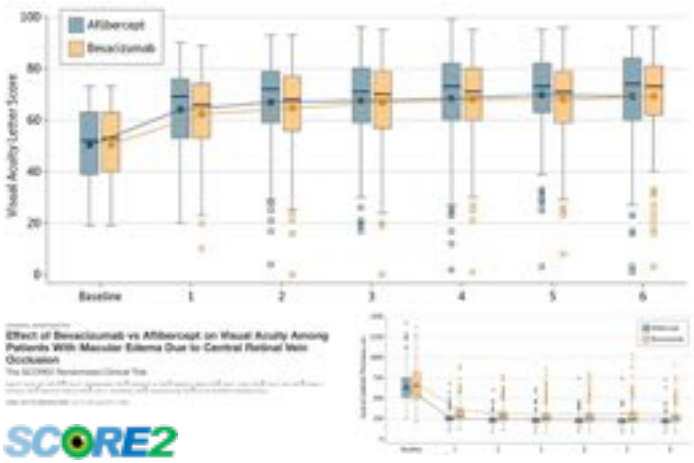
Même efficacité (AV, OM)



Chatziralli I & al. Graefes Arch Clin Exp Ophthalmol. juin 2017;255(6):1093-100.

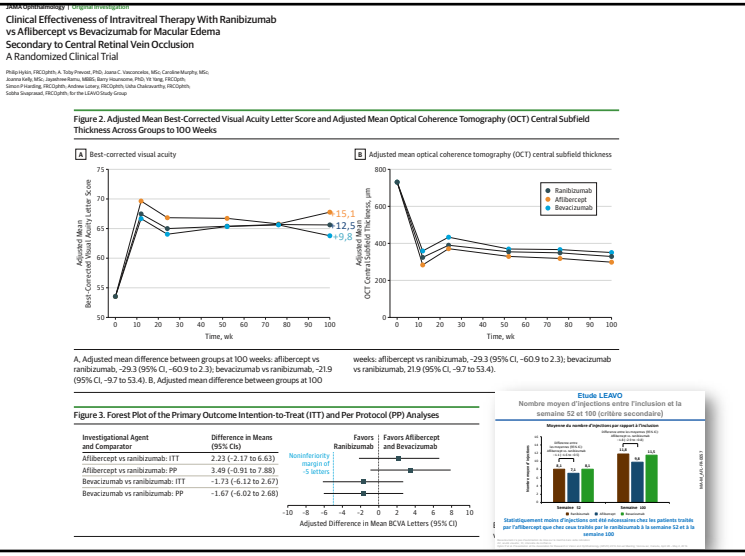
134

Même efficacité (AV, OM)



Scott IU & al. JAMA. 23 mai 2017;317(20):2072-87.

135



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Moins d'injections sous aflibercept (T&E)

INJECTION FREQUENCY OF AFLIBERCEPT VERSUS RANIBIZUMAB IN A TREAT-AND-EXTEND REGIMEN FOR CENTRAL RETINAL VEIN OCCLUSION

A Randomized Clinical Trial

MANUEL CASSELHOLM DE SALLES, MD, URBAN AMRÉN, MD, PhD, ANDERS KVANTA, MD, PhD, DAVID L. EPSTEIN, MD, PhD

OVCR, 45 patients naïfs
T&E après 3 injections (cappé)

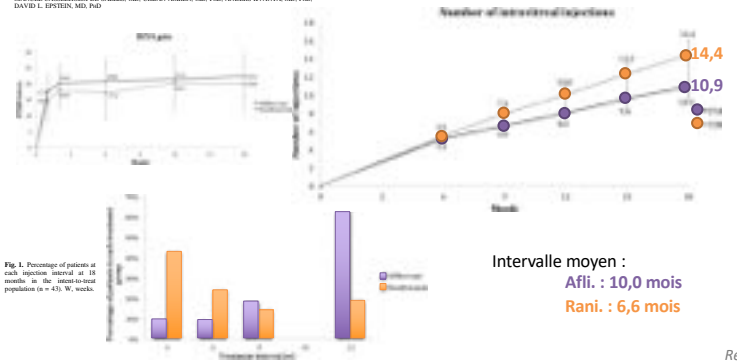

Fig. 1. Percentage of patients at each injection interval at 18 months in the intent-to-treat population (n = 43). W, weeks.

Intervalle moyen :
Afli. : 10,0 mois
Rani. : 6,6 mois

Retina. 2018 apr 5

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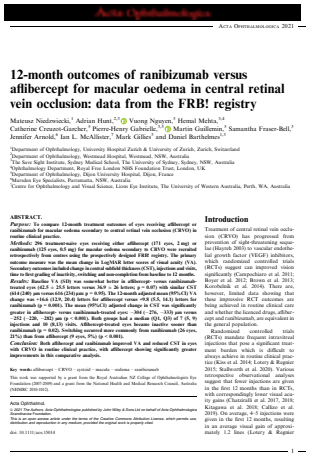
Etudes « IRL » en faveur de l'aflibercept…

Clinical science

Twelve-month outcomes of ranibizumab versus aflibercept for macular oedema in branch retinal vein occlusion: data from the FRB! registry

Adrian R Hunt, Vuong Nguyen, Catherine P Creuzot-Garcher, Socorro Alfaro, Pierre-Henry Gabrielle, Javier Zarranz-Ventura, Martin Guillemin, Samantha Fraser-Bell, Ricardo P Casaroli Marano, Jennifer Arnold, Ian L McAllister, Louise O'Toole, Mark C Gillies, Daniel Barthelmes, Hemal Mehta



Acta Ophthalmologica

Acta Ophthalmologica 2021

12-month outcomes of ranibizumab versus aflibercept for macular oedema in central retinal vein occlusion: data from the FRB! registry

Mateusz Nicdzwiecki, Adrian Hunt, Vuong Nguyen, Hemal Mehta, Catherine Creuzot-Garcher, Pierre-Henry Gabrielle, Martin Guillemin, Samantha Fraser-Bell, Jennifer Arnold, Ian L. McAllister, Mark Gillies and Daniel Barthelmes

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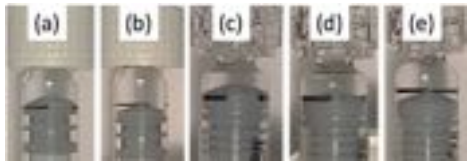
Influence de la présentation ?

ACCURACY AND PRECISION OF INTRAVITREAL INJECTIONS OF ANTI–VASCULAR ENDOTHELIAL GROWTH FACTOR AGENTS IN REAL LIFE

What Is Actually in the Syringe?

ITAMAR LOEWENSTEIN, MICHAELLA GOLDSTEIN, MD, JOSEPH MOISSEIEV, MD, ELAD MOISEIEV, MD

Pre-filled aflibercept syringes–variability in expressed fluid volumes and a case series of transient central retinal artery occlusions



Ranibizumab prefilled syringes: benefits of reduced syringe preparation times and less complex preparation procedures

Accepted Manuscript

The Impact of Prefilled Syringes on Endophthalmitis following Intravitreal Injection of Ranibizumab

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Choix du traitement

MODIFICATIONS DE TRAITEMENT ?

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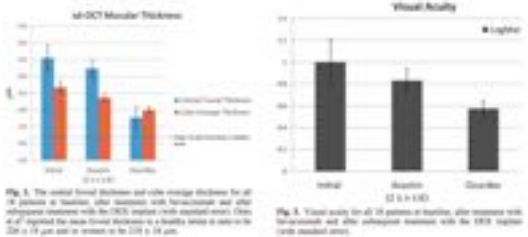
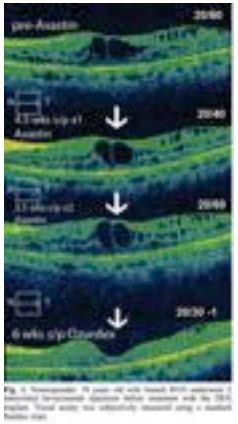
Modification inter-classes

RECALCITRANT MACULAR EDEMA AFTER INTRAVITREAL BEVACIZUMAB IS RESPONSIVE TO AN INTRAVITREAL DEXAMETHASONE IMPLANT IN RETINAL VEIN OCCLUSION





Retina. 2013;33(6):1227–31.

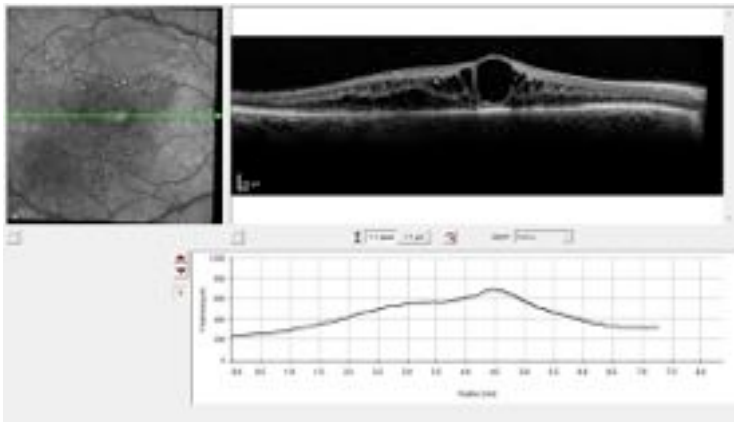
141

M. G, 73 ans

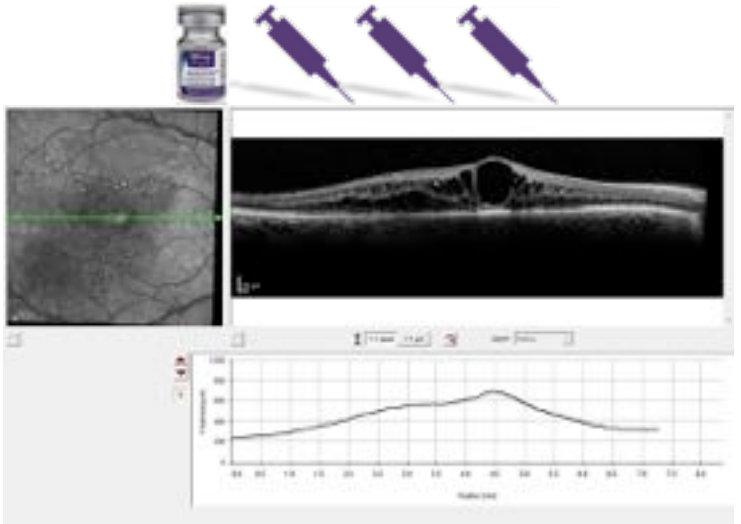
- Antécédents :
  - HTO sous brimonidine+timolol
- OVCR OD en mai 2010
  - Laser maculaire (???)
  - Janvier 2011, 1/20 : essai bevacizumab
    - Amélioration pendant 3 semaines
  - Mars 2011 : 2,5/10
    - Récidive OMC
    - mais part à l'étranger…

142

Juillet 2011 (OVCR>1an) : 2/10, P10 (16 mmHg)

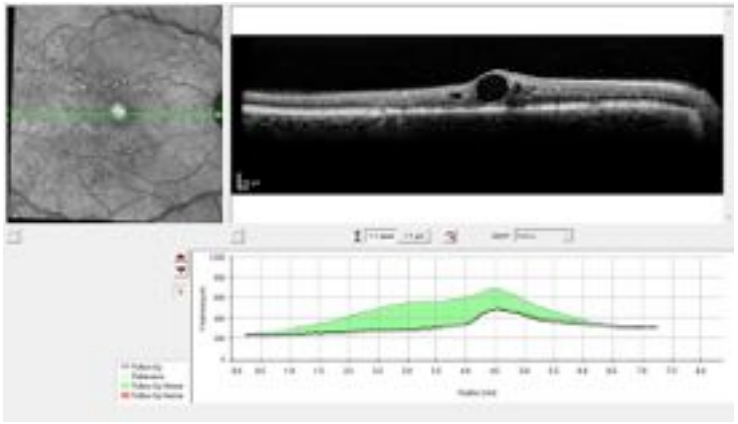


143



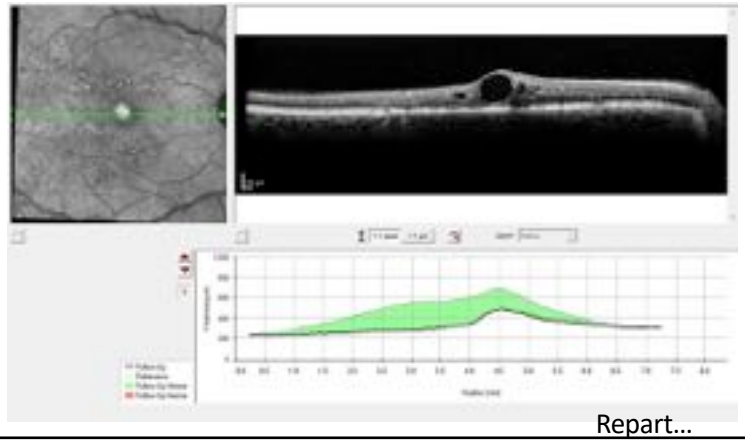
144

Octobre 2011 (1 mois après 3e) : 6/10 (22mmHg)



145

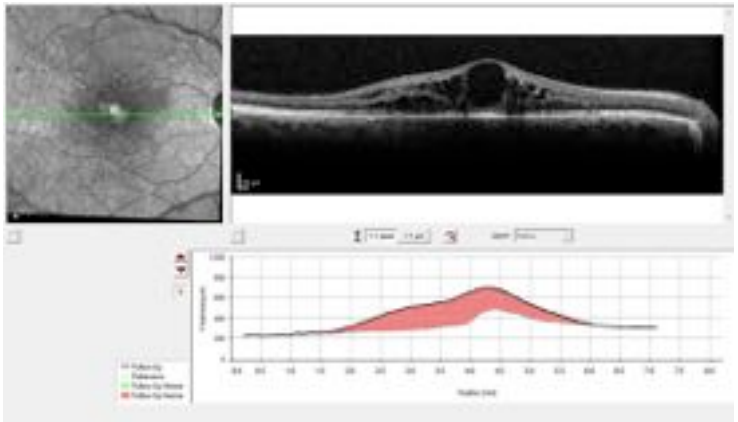
Octobre 2011 (1 mois après 3e) : 6/10 (22mmHg)



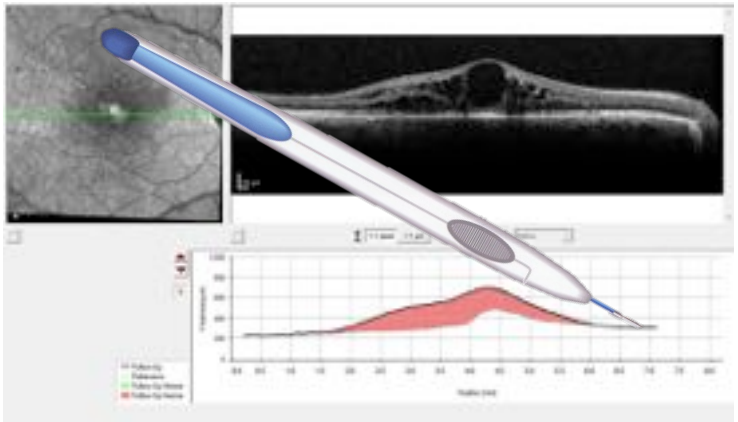
Repart…

146

Janvier 2012 : 0,15 à 0,2ff (23mmHg)

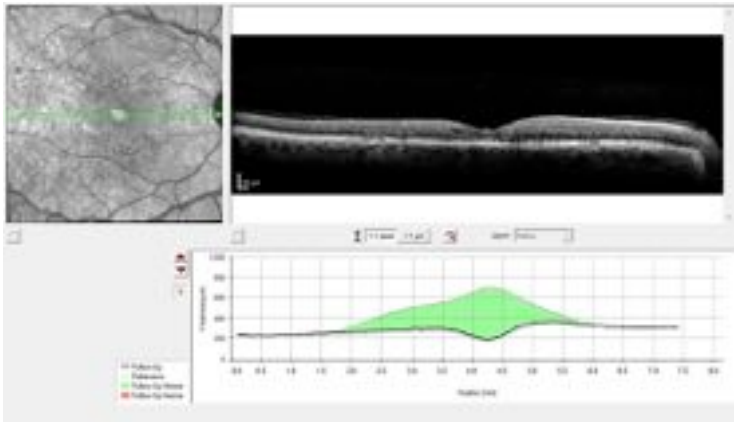


147



148

Mars 2012 (+2M) : 6/10 (35mmHg)

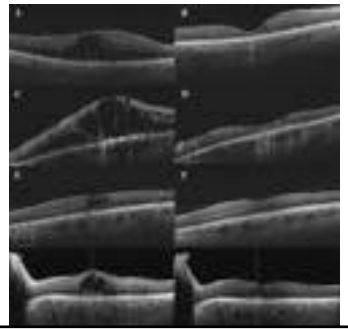


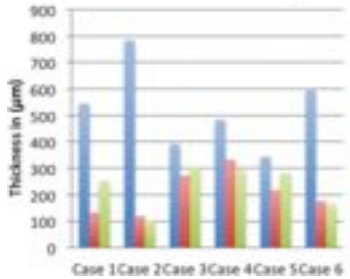
149

… Ou d'un anti-VEGF à l'autre

RESPONSE TO AFLIBERCEPT AS SECONDARY THERAPY IN PATIENTS WITH PERSISTENT RETINAL EDEMA DUE TO CENTRAL RETINAL VEIN OCCLUSION INITIALLY TREATED WITH BEVACIZUMAB OR RANIBIZUMAB

JAMES A. EADIE, MD, MICHAEL S. IP, MD, AMOL D. KULKARNI, MD



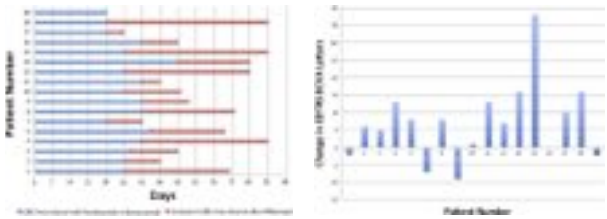


. Retina 2014;34:2439–43

150

Ophthalmic Res 2015;54:150–6

Aflibercept for Previously Treated Macular Edema Associated with Central Retinal Vein Occlusions: 1-Year Results of the NEWTON Study



Ophthalmology Retina 2018;2:128–33

151

Combiner corticoïde et anti-VEGF ?

EFFECT OF COMBINATION THERAPY WITH BEVACIZUMAB AND DEXAMETHASONE INTRAVITREAL IMPLANT IN PATIENTS WITH RETINAL VEIN OCCLUSION

CLEARSIDE BIOMEDICAL

Clearside Biomedical Announces SAPPHIRE Phase 3 Study of Combination Therapy in Retinal Vein Occlusion Did Not Meet Its Primary Endpoint

152

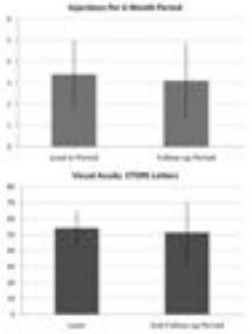
Traitement de l'œdème maculaire

ET LE LASER ?

153

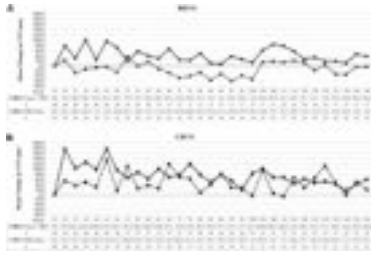
PPR : aucune influence sur l'OM

PROSPECTIVE STUDY OF PERIPHERAL PANRETINAL PHOTOCOAGULATION OF AREAS OF NONPERFUSION IN CENTRAL RETINAL VEIN OCCLUSION



Scatter Photocoagulation Does Not Reduce Macular Edema or Treatment Burden in Patients with Retinal Vein Occlusion

The RELATE Trial



Retina. 2013 Jan;33(1):56–62

Ophthalmology. 2015 Jul;122(7):1426–37

154

Grille maculaire et OVCR : aucun effet sur l'AV

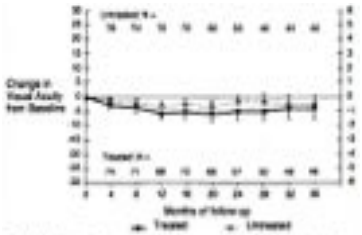
Evaluation of Grid Pattern Photocoagulation for Macular Edema in Central Vein Occlusion

The Central Vein Occlusion Study Group M Report

The Central Vein Occlusion Study Group*

Diminution diffusions angiographiques

Pas d'amélioration AV



155

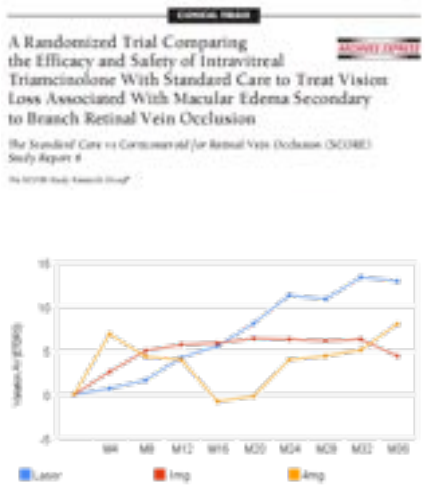
Grille maculaire et OBVR

- Gain moyen d'AV : **+1,3 lignes** ETDRS (vs 0,2)
- AV > 5/10 : **60%** (vs 34%)
- Gain de 2 lignes : **65%** (vs 37%)
- Amélioration plus importante si traitement durant la première année d'évolution
  - Mais toujours observée dans 53% des yeux si traitement plus tardif

Indication : AV < 5/10, après résorption des hémorragies, au delà de 3 mois d'évolution, sans ischémie maculaire

156

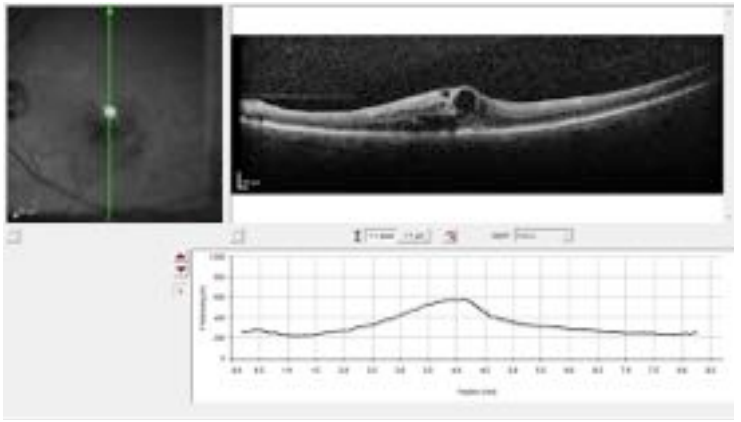
Argon laser photocoagulation for macular edema in branch vein occlusion. The Branch Vein Occlusion Study Group.



A Randomized Trial Comparing the Efficacy and Safety of Intravitreal Triamcinolone With Standard Care to Treat Vision Loss Associated With Macular Edema Secondary to Branch Retinal Vein Occlusion

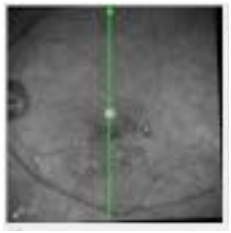
157

2 septembre 2011 (3 mois d'évolution)



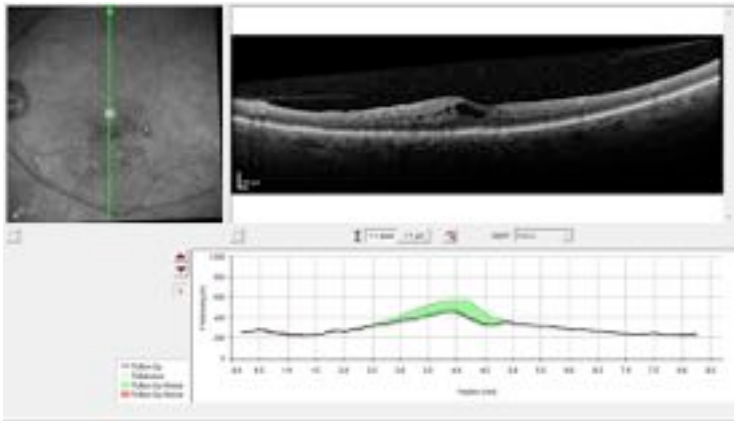
158

-> hémi-grille inférieure

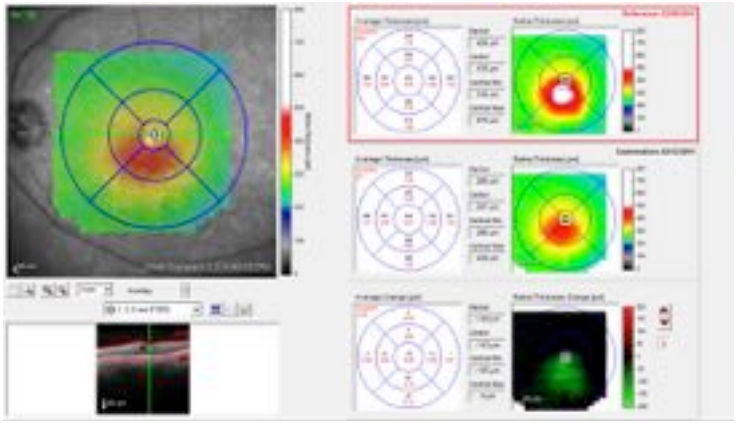


159

9 décembre 2011 (Laser +3M)

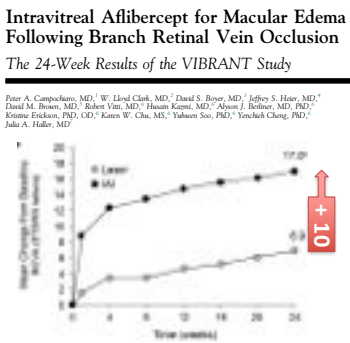


160



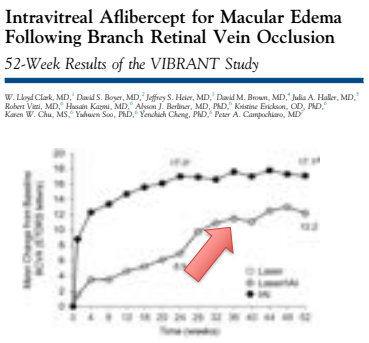
161

OBVR : Anti-VEGF > grille maculaire



Intravitreal Aflibercept for Macular Edema Following Branch Retinal Vein Occlusion

The 24-Week Results of the VIBRANT Study



Intravitreal Aflibercept for Macular Edema Following Branch Retinal Vein Occlusion

52-Week Results of the VIBRANT Study

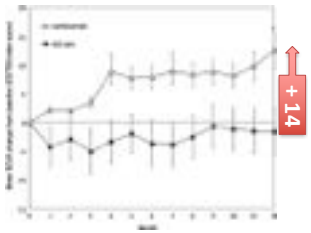
Ophthalmology. 2016 Feb;123(2):330–6.

162

OBVR : Anti-VEGF > grille maculaire

Randomized Controlled Trial of Intravitreal Ranibizumab Versus Standard Grid Laser for Macular Edema Following Branch Retinal Vein Occlusion

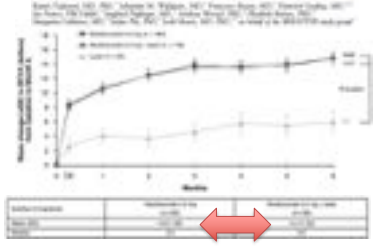
MEI HONG TAN, IAN L. MCALLISTER, MARK E. GILLIES, NITIN VERMA, GAYATRI BANERJEE, LYNNE A. SMITHIES, WAN-LING WONG, AND TIEN Y. WONG



Am J Ophthalmol. 2014 Jan;157(1):237–47.e1.

Individualized Stabilization Criteria–Driven Ranibizumab versus Laser in Branch Retinal Vein Occlusion

Six-Month Results of BRIGHTER



Ophthalmology. 2016 Jun;123(6):1332-44.

163

Grille maculaire : seconde intention

- Démarrer le traitement par injections intra-vitréennes
  - Amélioration AV rapide
- Grille maculaire envisageable pour éviter répétitions des injections
  - OM > 3 mois
    - Diffusions angiographiques
  - AV < 5/10
  - Après résorption des hémorragies

164

Technique de la photocoagulation en grille maculaire

- Laser vert, rouge ou infrarouge
- Verre central du V3M, « Centralis Direct® », « Area Centralis® »…
- Impacts de **100µ**, Durée courte **≤ 0,1 s**
- Puissance nécessaire pour impacts à peine visibles
- Non confluents (espacement de 1 à 2 impacts)
- Uniquement dans l'aire d'épaississement rétinien et de diffusions
- En restant à plus de 1/2 diamètre papillaire (750µ) du centre de la macula.

165

Intérêt du laser infra-liminaire ?


Biomedicine & Pharmacotherapy 97 (2018) 293–299

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha

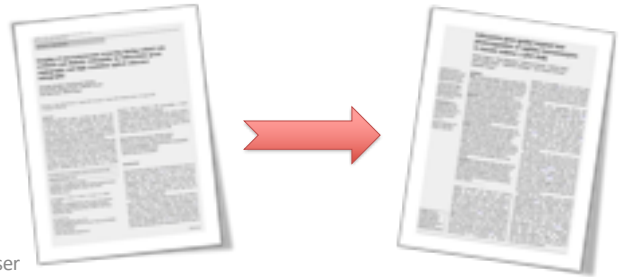
Review

Subthreshold diode micropulse laser versus conventional laser photocoagulation monotherapy or combined with anti-VEGF therapy for diabetic macular edema: A Bayesian network meta-analysis

Ying Wu[a], Pu Ai[b], Zisheng Ai[c,*], Guotong Xu[d,*]

Conclusion: There was no apparent difference on improving vision between SDMLP monotherapy and CLP monotherapy. The most effective treatment in the network was ranibizumab therapy combined with CLP followed by SDMLP monotherapy, Bevacizumab therapy combined with CLP, and CLP monotherapy in rank order.

166



Place du laser

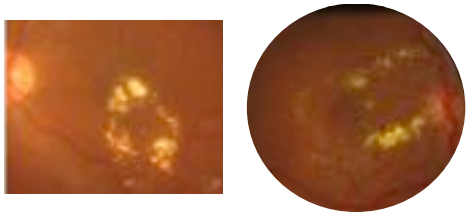
PHOTOCOAGULATION CIBLÉE

167

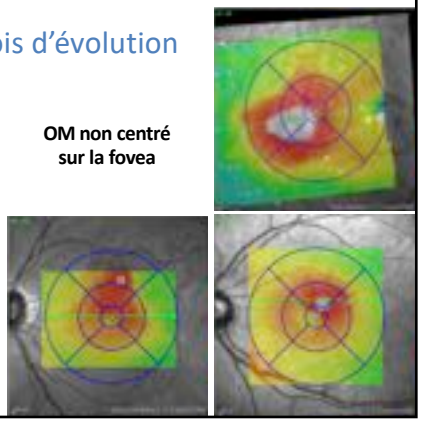
Quand suspecter des TelCaps ?

- OMD récidivant
- OVR (OBVR > OVCR) ancienne > 6 mois d'évolution

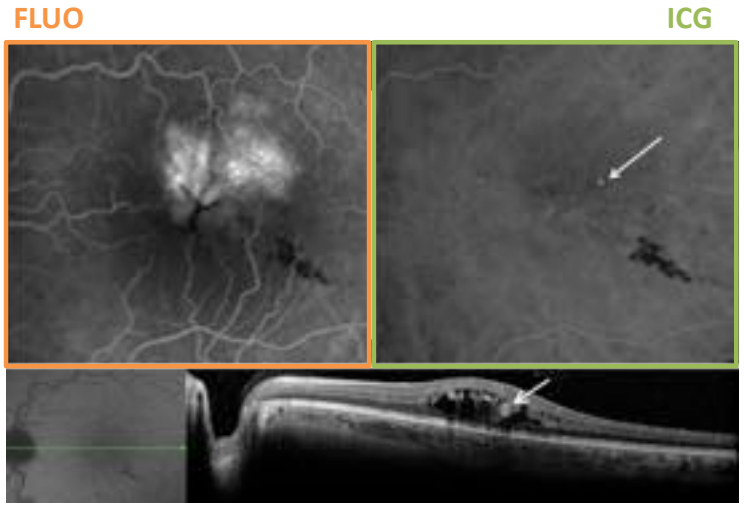
Présence d'exsudats



OM non centré sur la fovea

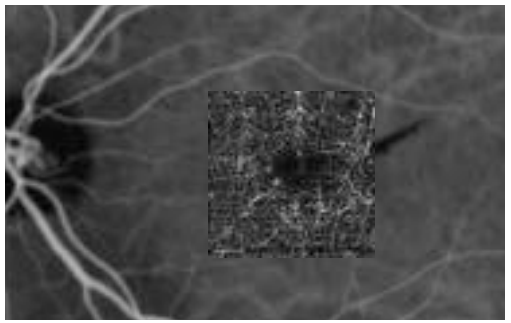


168

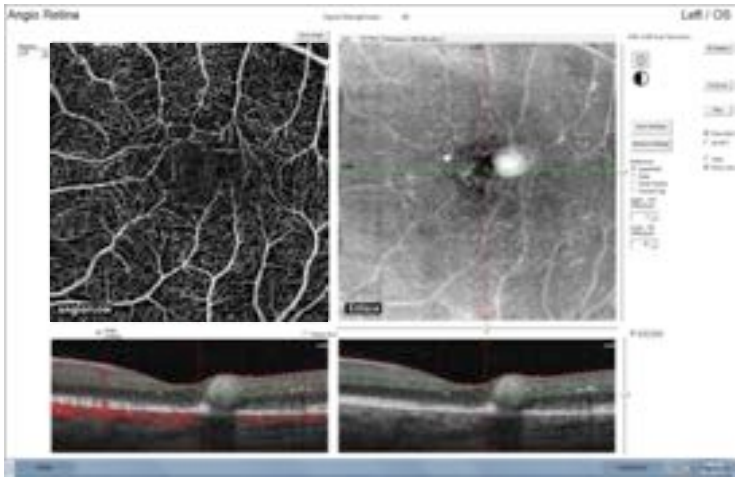


169

OCT-A peu contributif



170



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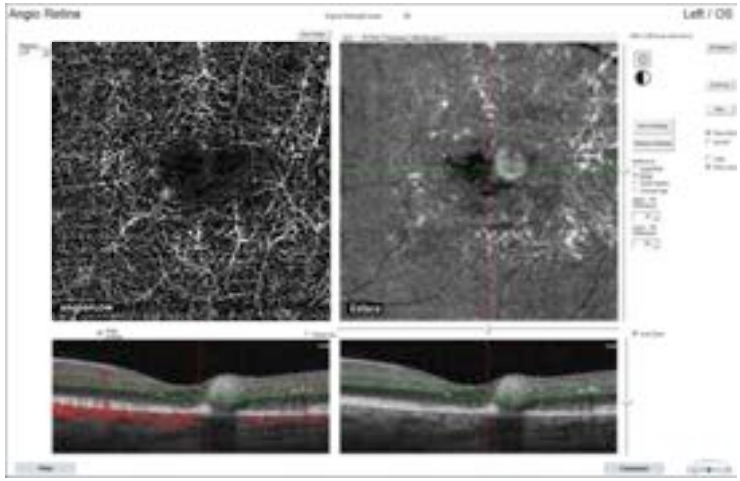
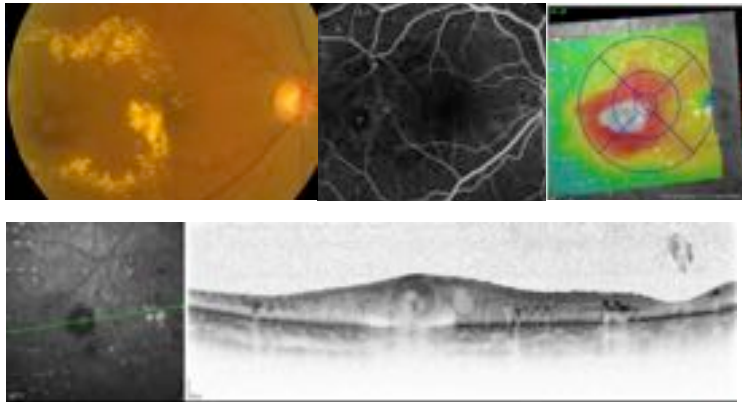


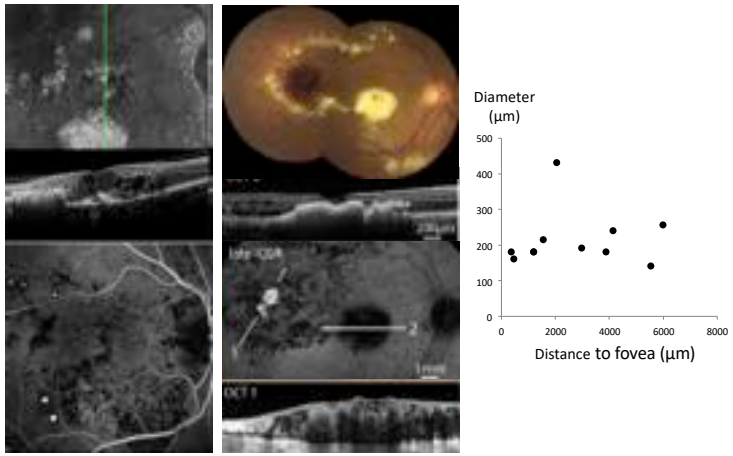
172

Parfois éloignés de la fovea



173

Diamètre / distance de la fovea



DME RVO

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Fréquence des TelCaps ?

- Incidence augmente avec la durée et la gravité de l'œdème maculaire
- OVR chronique
  - BRVO: 37% à 64%
  - OVCR : 24% à 38%
- Plus fréquent si exsudats (78 vs 41%)
- OMD : 63%
  - 100% des yeux avec exsudats

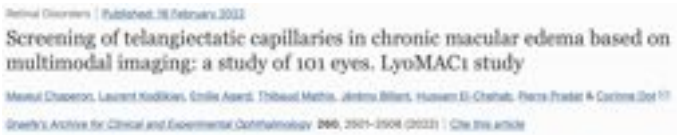

Indocyanine green angiography for identifying telangiectatic capillaries in diabetic macular oedema

British Journal of Ophthalmology 2020;104:509-513.

175

Fréquence des TelCaps ?

- Incidence augmente avec la durée et la gravité de l'œdème maculaire


Screening of telangiectatic capillaries in chronic macular edema based on multimodal imaging: a study of 101 eyes. LyoMAC1 study

66,3%

British Journal of Ophthalmology 2020;104:509-513.

176

Photocoagulation directe des macroanévrysmes

- ***Guidée par l'angiographie ICG ou l'OCT***
- Laser 532nm ou 577nm
- Verre type Centralis Direct®, Area Centralis®…
- Impacts de **(25) 50 à 100µ**
  - focalisés sur les macroanévrysmes (et non sur l'EP)
- Durée plus ou moins longue (selon mouvements du patient), **≥ 0,1s**
  - **OU très courts, en RAFALE ?**
- Puissance suffisante pour obtenir un changement de coloration
  - ≈ 100 mW, le plus souvent <200 mW
- ***Contrôle immédiat de l'efficacité en OCT***

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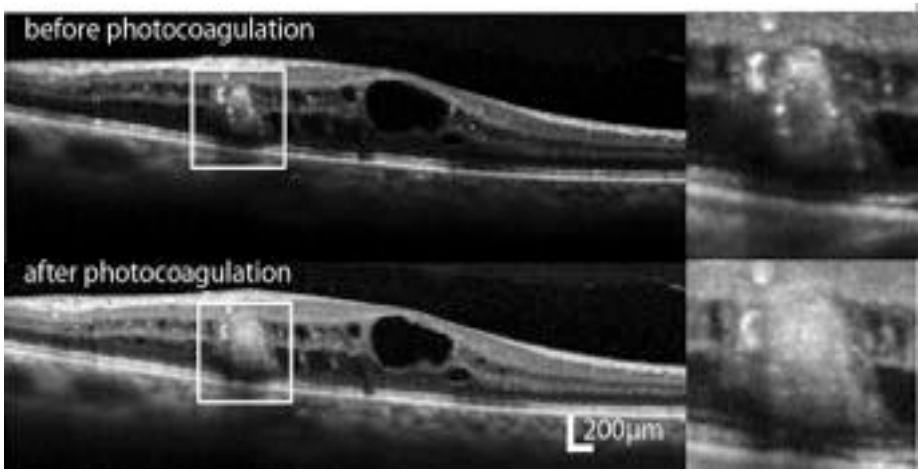
Contrôle immédiat en OCT



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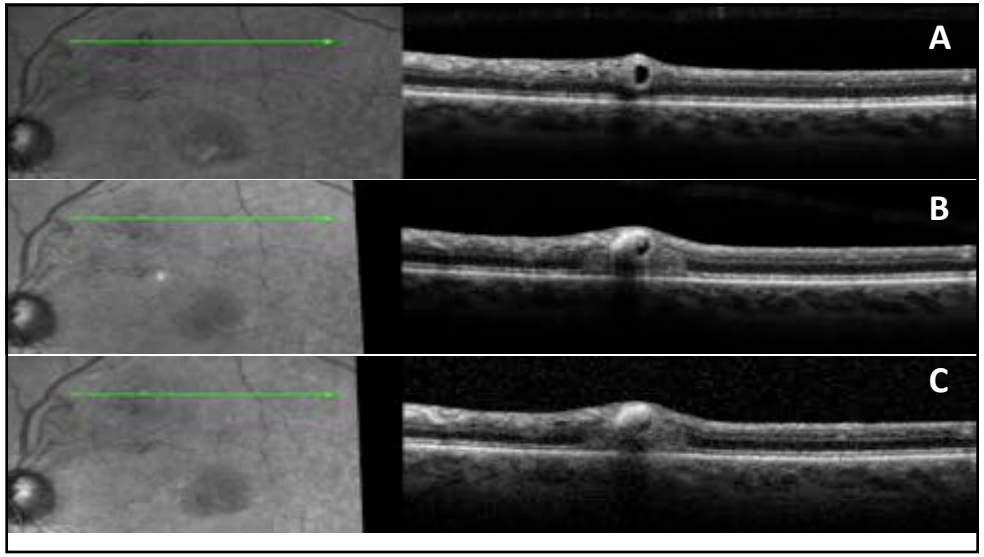

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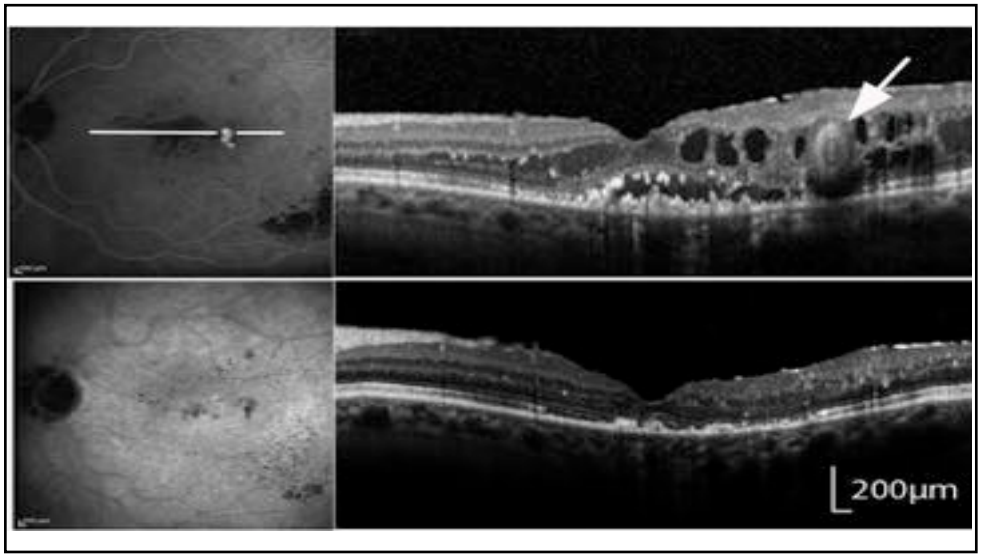
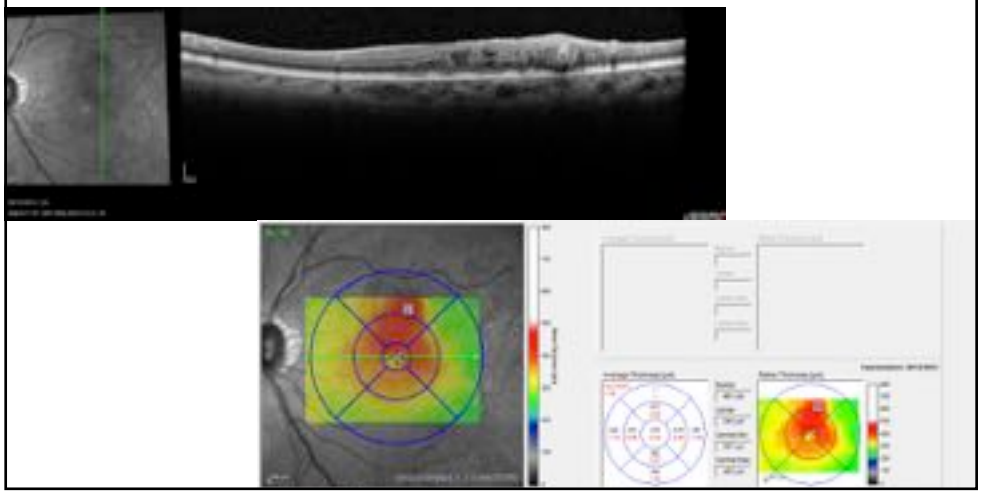


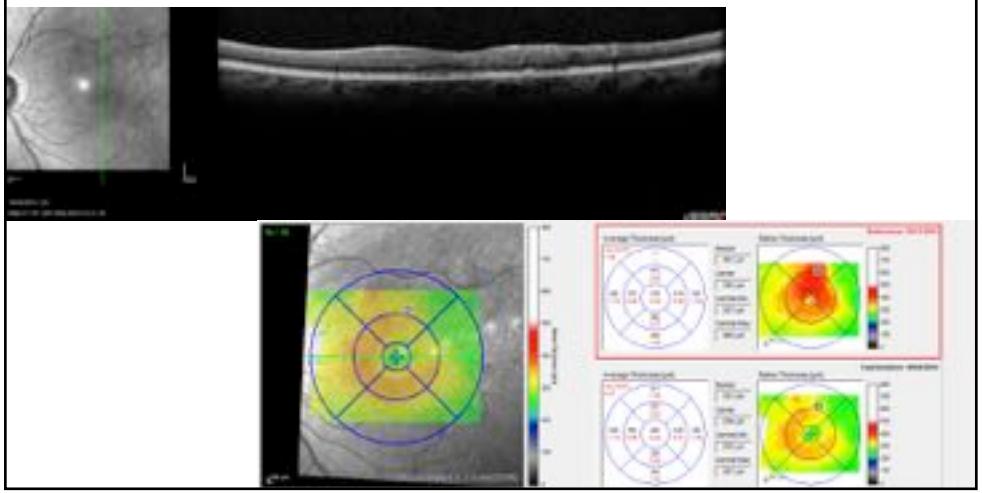
180

Juste après…



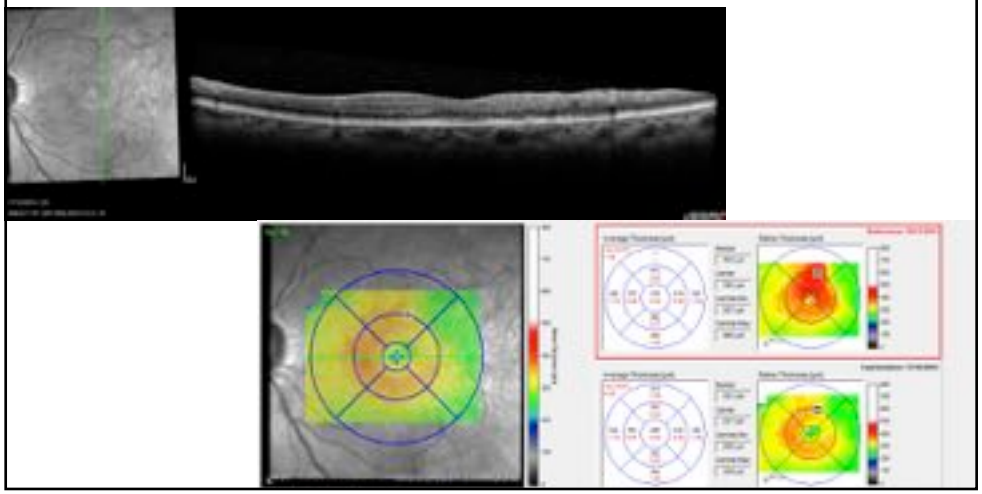
181

+ 4 mois



182

+ 10 mois



183

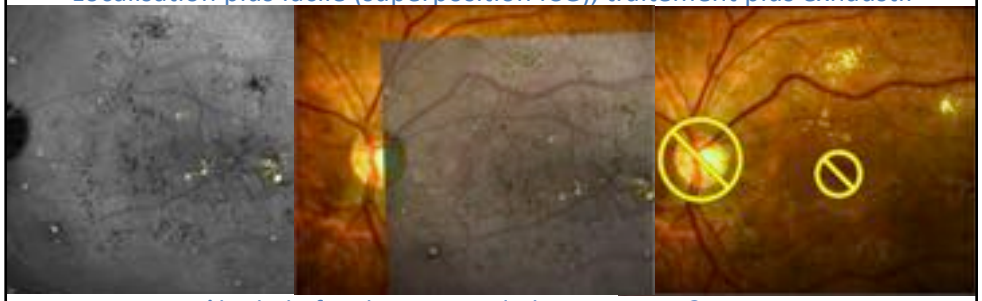
… Mais ce n'est pas toujours si simple !

- **/!\ Risque de néovascularisation /!** (Lésion de la membrane de Bruch/EP)
  - Contre-indication en cas de drusen / DMLA
  - Minimisé par
    - faible taille d'impact
    - focus à la surface du MA
    - Avant IIV (MA plus éloigné de l'EP)
    - puissance la plus faible efficace
- Parfois difficile à localiser
  - … ou à retrouver au FO d'après l'angiographie
- Risque de lésion fovéolaire en cas de mauvaise fixation
- Risque d'élargissement des cicatrices juxta-fovéolaires

184

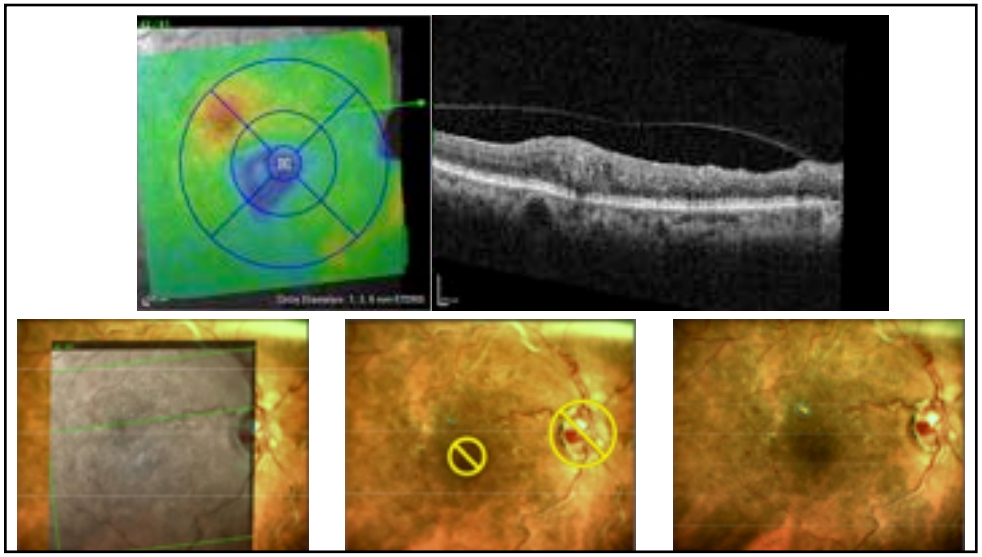
Place du laser guidé (Navilas®) ?

- Localisation plus facile (superposition ICG), traitement plus exhaustif

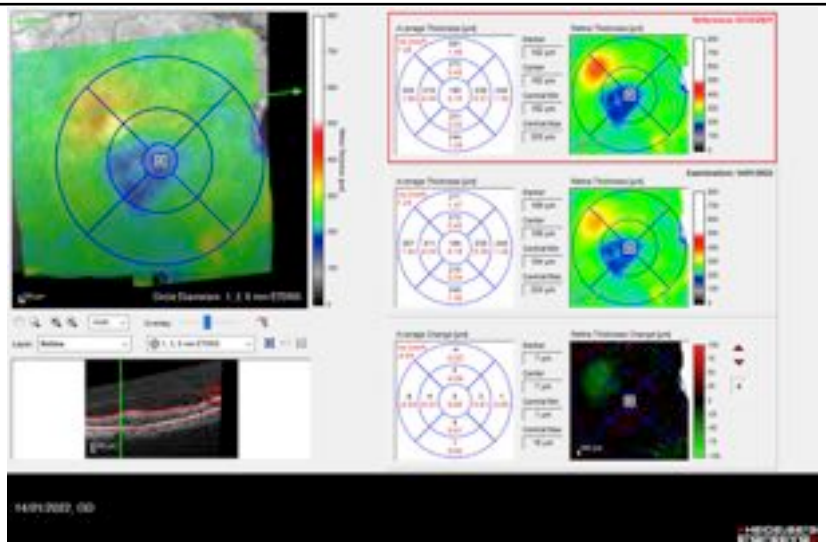


- Mais contrôle de la focalisation et de la puissance ?
  - Plutôt en l'absence d'OM contrairement au traitement « manuel » ?

185



186



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Etude pilote

Case	Sex/age/cause of visual loss	Duration of vision loss	Number of targets	Largest target (µm)	Distance to fovea (µm)	Initial VA	VA at 6 months	Initial foveal thickness (µm)	Foveal thickness at 6 months
1	F/51/DME	1 year	RE: 8 LE: 5	RE: 250 LE: 410	RE: 435 LE: 442	20/200 OU	RE: 20/200 LE: 20/50	RE: 582 LE: 742	RE: 208 LE: 264
2	F/60/DME	5 years	1	360	1384	20/200	20/200	681	177
3	M/62/DME	Unknown	1	495	4613	20/400	20/100	256	208
4	M/65/RVO	5 years	1	420	6220	20/400	20/200	371	264
5	F/70/RVO	5 years	2	430	2550	20/30	20/30	304	191
6	M/63/RVO	1 month	1	477	1741	20/50	20/30	560	152
7	F/72/RVO	1 year	1	284	1675	20/60	20/40	380	137
8	F/69/RVO	3 years	8	158	1620	20/100	20/60	902	620
9	M/64/RVO	5 years	2	180	552	20/40	NA	615	NA
10	F/66/DME	Unknown	2	172	620	20/200	NA	313	NA

- Etude rétrospective (CHNO des 15-20 ; Hôpital Lariboisière)
- 11 yeux de 6 femmes / 4 hommes (OMD : 4, OVR : 6)
- Durée d'évolution de 1 mois à 5 ans (médiane : 4 ans)
  - Tous avec exsudats, 4 déjà traités (IIV, laser maculaire)
- AV : 20/400 – 20/20 (médiane : 20/200)
- 1 à 8 macroanévrysmes >150µm (médiane : 2)
- Taille de 158µ à 603µ (médiane : 410µm)

Paques & al. British Journal of Ophthalmology 2017;**101**:170-174.

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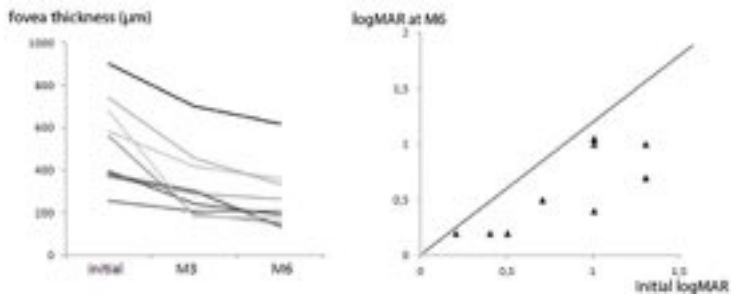
6 mois après photocoagulation



528µm (± 200) vs 271µm (±152)
(p<0.05)

0.82 vs 0.58
(p<0.05)

Soit +2,4 lignes (+12 lettres) ETDRS

Pagues & al. British Journal of Ophthalmology 2017;**101**:170-174.

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Essai prospectif randomisé en cours : TaLaDME

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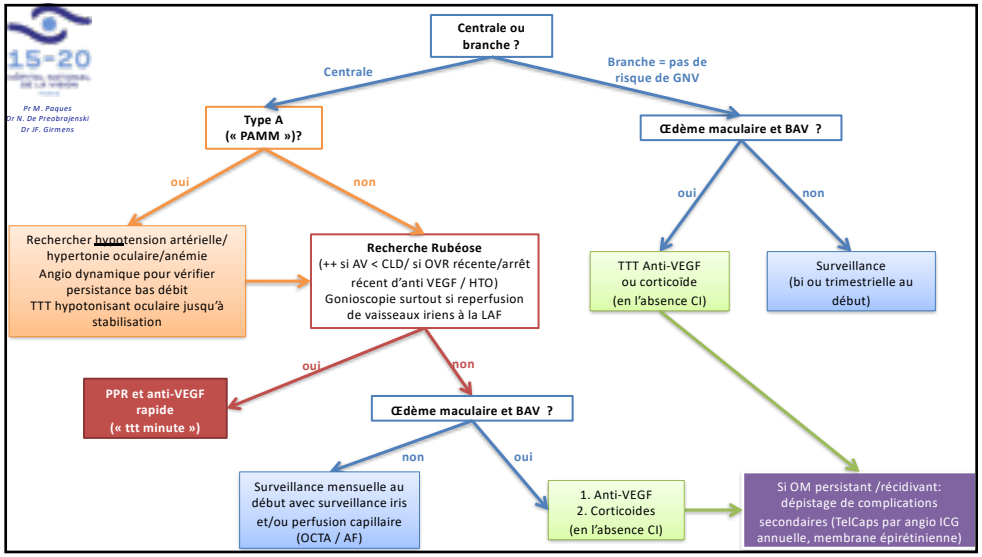

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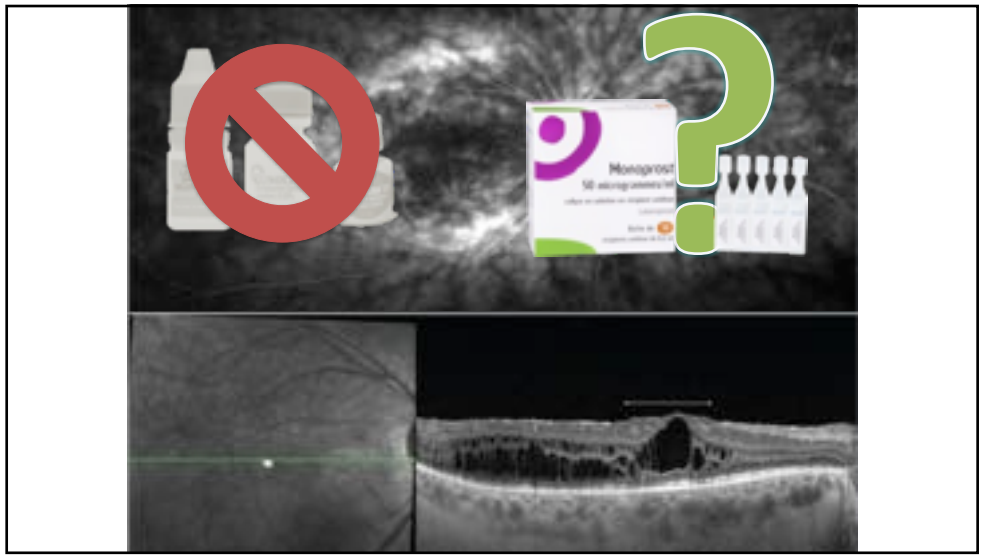

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Guidelines for the Management of Retinal Vein Occlusion by the European Society of Retina Specialists (EURETINA)

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Occlusions veineuses rétiniennes
Retinal vein occlusion

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