

Corticothérapie en rétine médicale

Retour sur 15 ans d'expérience



Laurent KODJIKIAN

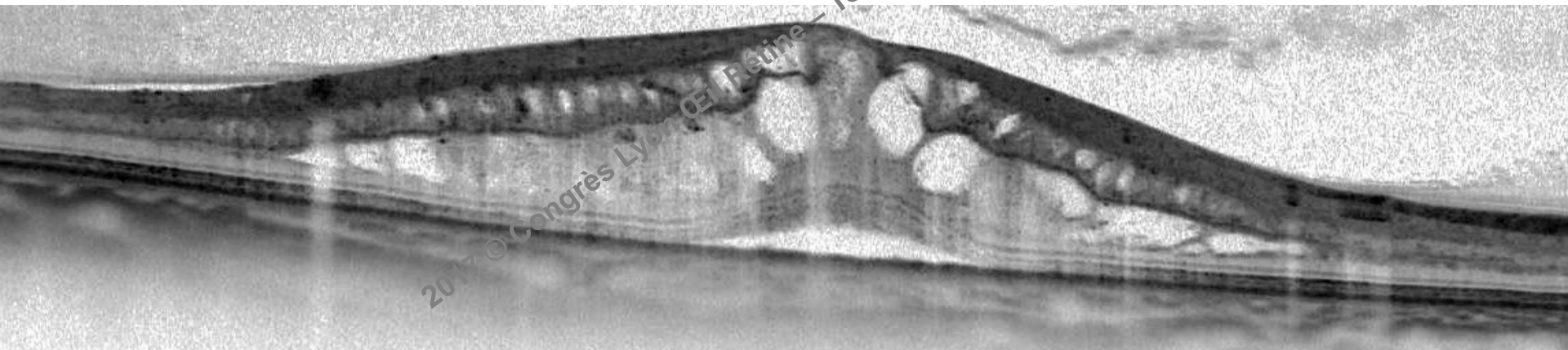
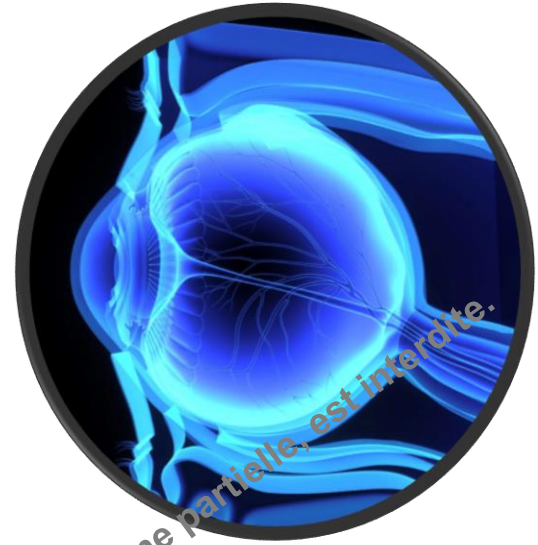
CHU de la CROIX-ROUSSE
UMR-CNRS 5510 Matéis
Lyon, France



Hôpitaux de Lyon

Déclaration d'intérêts

- AbbVie
- Alcon
- Allergan
- Bayer
- Horus
- Kryos
- Roche
- Novartis
- Théa



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CAS CLINIQUES

- DEXA utilisé d'emblée
- DEXA utilisé en seconde intention (switch)
- Tolérance DEXA

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Merci à David Bellocq et Amina Rezkallah

10 M.D agé de 65 ans, DNID depuis 17 ans, ADO-NIR, suivi médical irrégulier

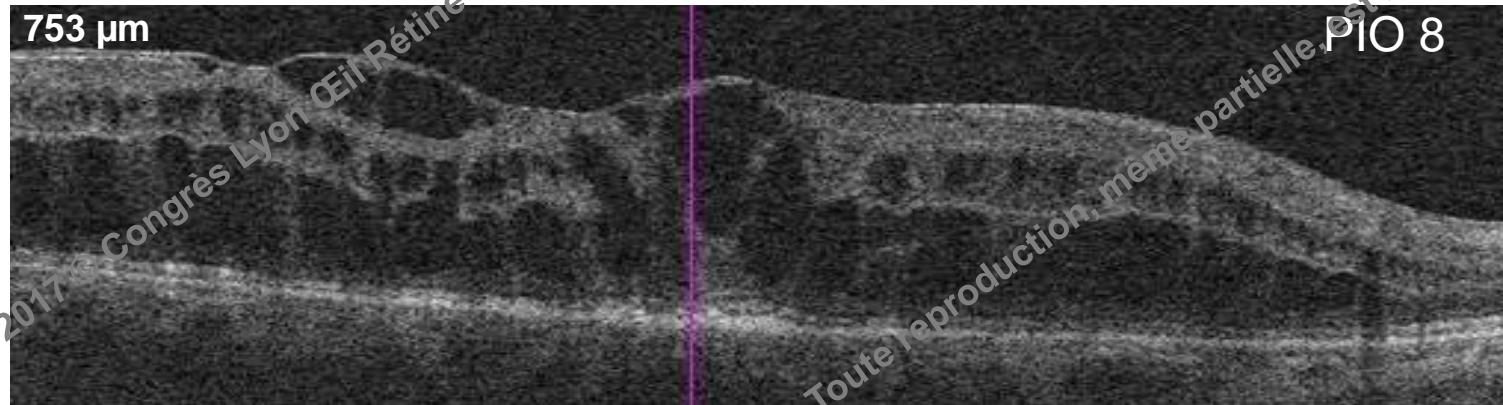
☞ HbA1c = 8,7%, TA équilibrée

☞ AV OD = 34L (lettres ETDRS)

☞ Pseudophake

☞ FO: RDNP sévère avec PRP 360°

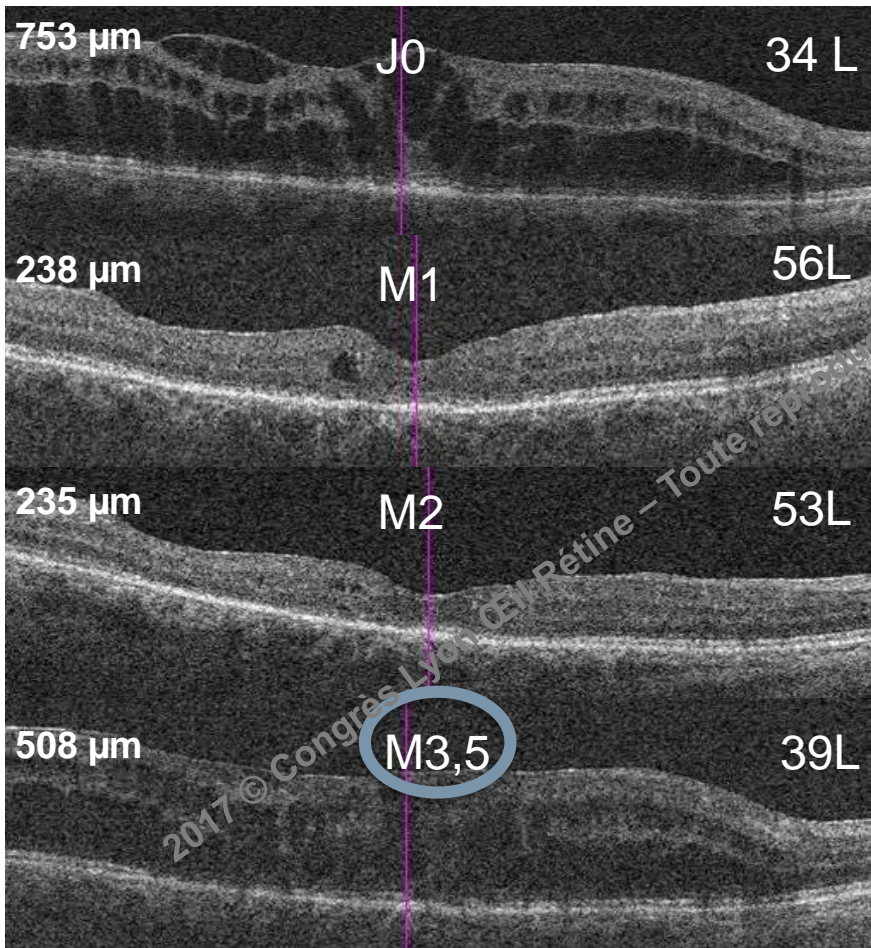
☞ OCT OD:



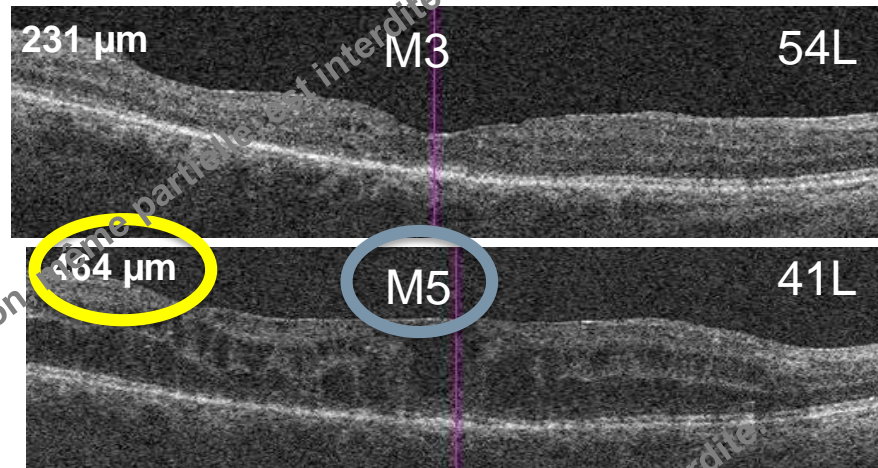
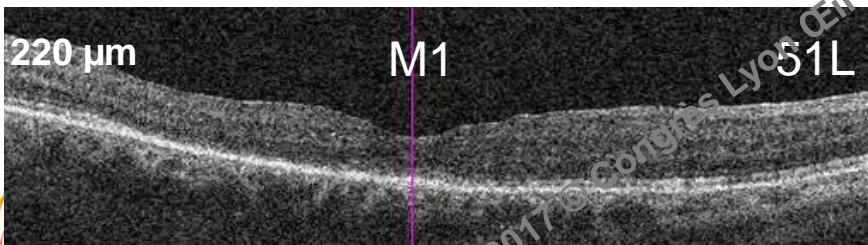
Indication IVT DEXA en 1^{ère} ligne car

- patient pseudophake,
- sans antécédent de glaucome
- au suivi médical irrégulier

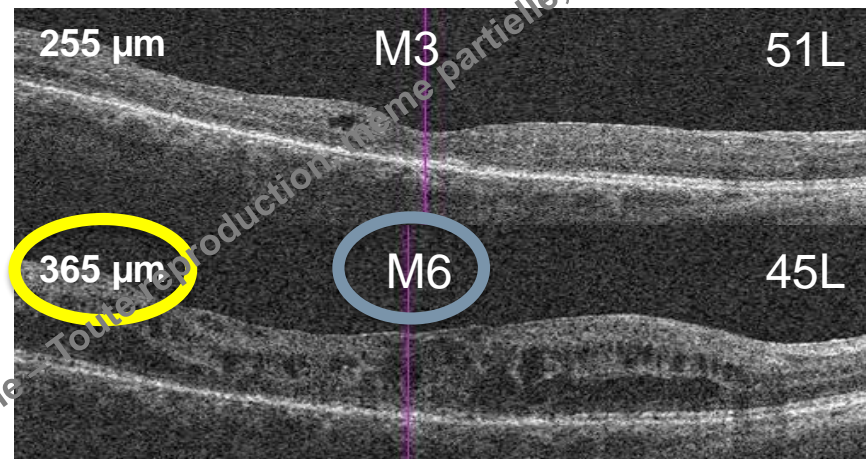
DEXA n°1 04/10/13 (HbA1c= 8,5%)



DEXA n°2 15/01/14 (HbA1c= 7,9%)



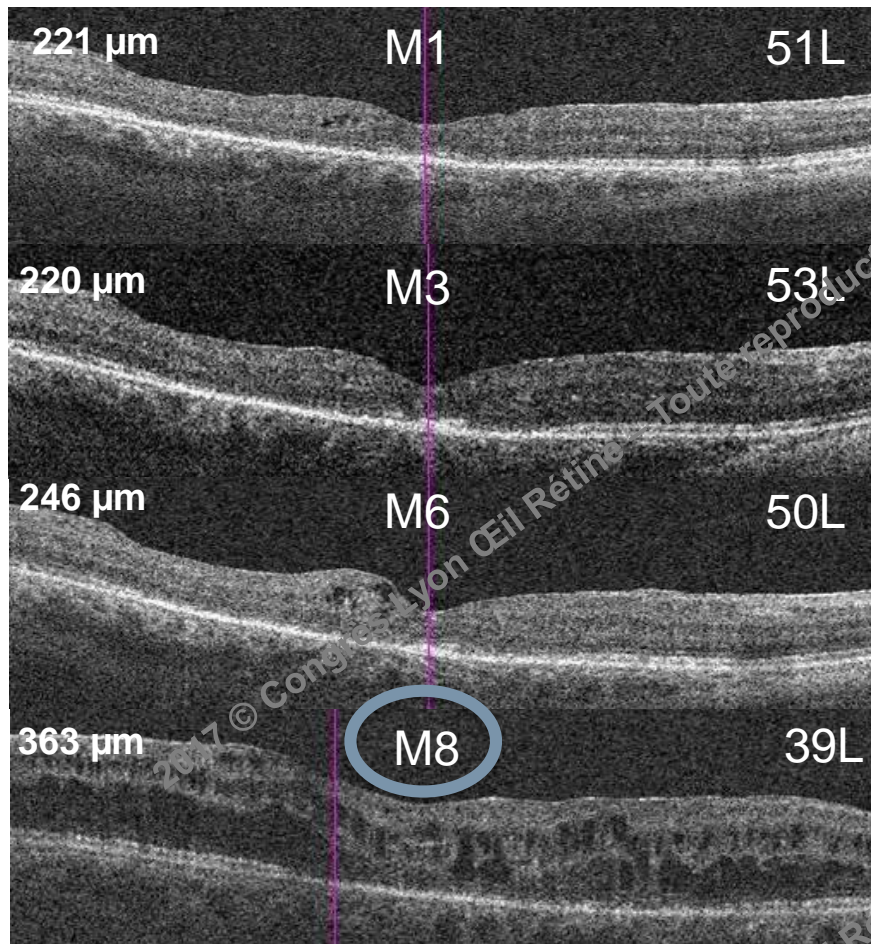
DEXA n°3 13/06/14 (HbA1c= 7,9%)



DEXA n°4 16/12/14 (HbA1c= 8,2%)



DEXA n°4 16/12/14 (HbA1c= 8,2%)



DEXA n°5 le 19/08/15 (HbA1c = 8,1%)

- AV initiale : 34 L
- AV maximale : 56 L
- AV stabilisée : 50 à 53 L
- Impression **d'augmentation des délais de récidence** avec 8 mois entre les deux derniers DEXA
- **5 IVT en 2 ans**
- Idéal pour les patients **au suivi régulier difficile**
- Pas de perte d'efficacité au cours du temps
- Pas d'hypertonie après 5 IVT/2 ans

LONG TERM EFFICACY OF DEXA – RELDEX STUDY (RETINA 2017): 3 YEARS

REAL-LIFE STUDY IN DIABETIC MACULAR EDEMA TREATED WITH DEXAMETHASONE IMPLANT

The Reldex Study

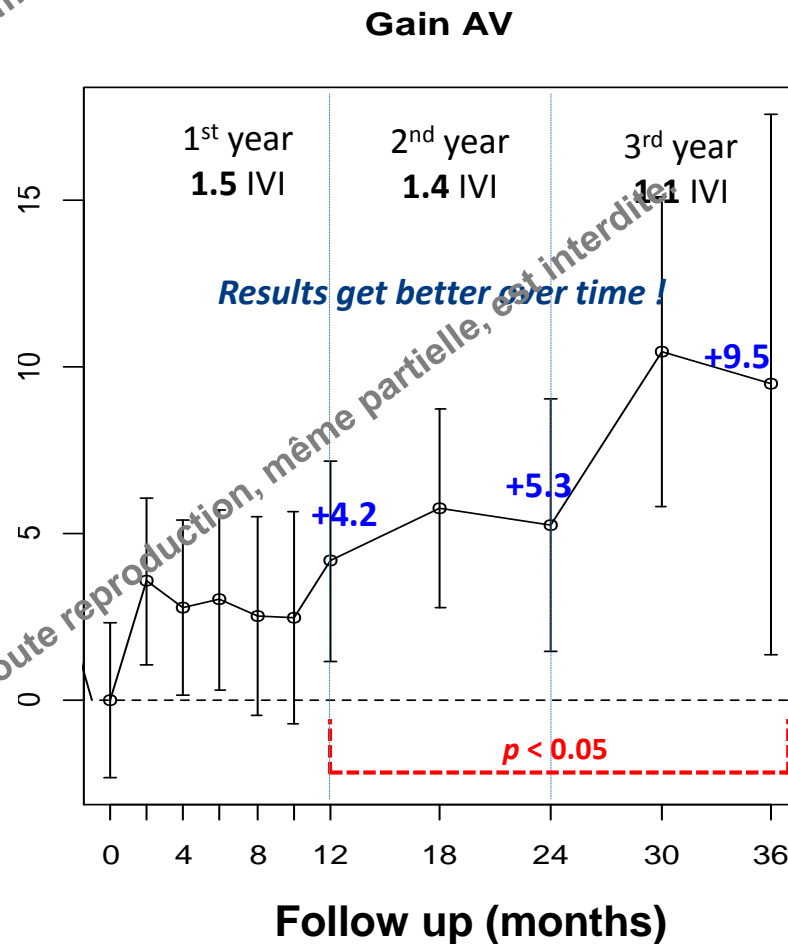
ARIANE MALCLÈS, MD,* CORINNE DOT, MD, PhD,† NICOLAS VOIRIN, PhD,*
ÉMILIE AGARD, MD,‡ ANNE-LAURE VIÉ, MD,* DAVID BELLOCQ, MD,* PHILIPPE DENIS, M
LAURENT KODJIKIAN, MD, PhD*

Purpose: To evaluate the efficacy and safety of intravitreal implant of dexamethasone (Ozurdex) in diabetic macular edema in real-life practice.

Intervalle moyen entre les injections (mois) [écart-type]	
Nombre total	7,3 (6,5-8,1)
La 1 ^{re} année	5,7 (4,8-6,7)
La 2 ^e année	7,5 (6,5-8,5)
La 3 ^e année	10 (8,1-11,9)

RETINA 37:753-760, 2017

VA Gain (letters) and 95% CI



Mixed effect linear model with time taken into account on a non-parametric basis

Cas clinique

Homme 72 ans

DT2 > 20 ans

Pas de GPAO

HbA_{1c} 7%



OD

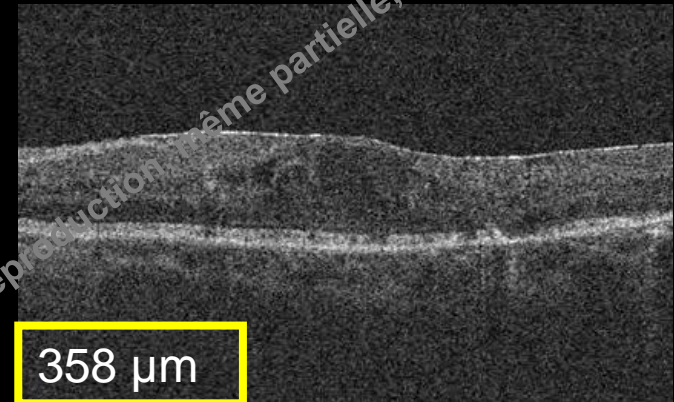
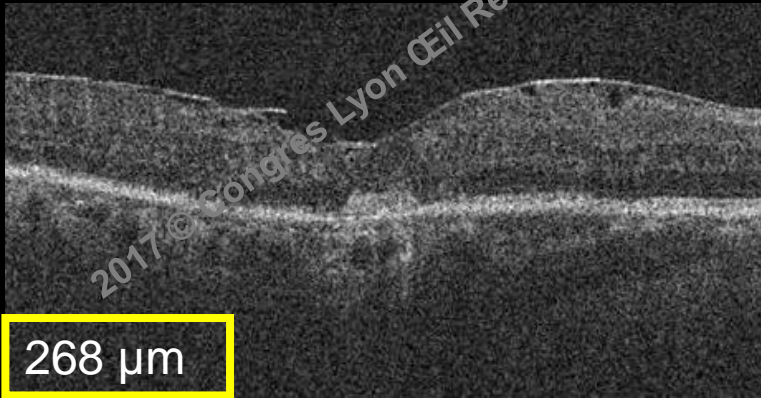
PKE Bosnie 2012
Perte fonctionnelle sur RDP et
exsudat central
PRP complète

OG

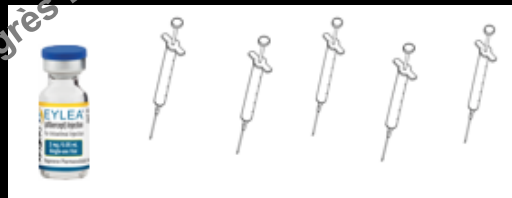
PKE 2012
RDNP
PRP à compléter
MER OG

EXAMEN

	OD	OG
AV	VBLM à 3 mètres	5/10 Ro1/4
PIO	12 mmHg	11 mmHg
SEGMENT ANTÉRIEUR	Calme Pas de rubéose irienne	

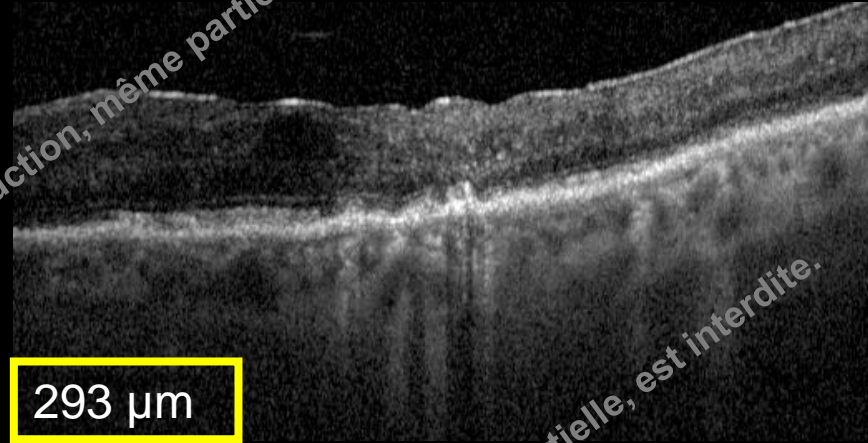


INDICATION DOSE DE CHARGE DE 5 IVT AFLIBERCEPT OG



M1 POST 3 IVT AFLIBERCEPT

	OG
AV	5/10 Ro1/4
PIO	13 mmHg
SEGMENT ANTÉRIEUR	Calme Pas de rubéose nienne



PRISE EN CHARGE ?

**Amélioration anatomique (seulement)
POURSUITE IVT 4 ET 5**



M1 POST 5 IVT AFLIBERCEPT

	OG
AV	5/10 Ro1/3 – stable ✓
PIO	12 mmHg
SEGMENT ANTÉRIEUR	Comme Pas de rubéose irienne



PRISE EN CHARGE ?

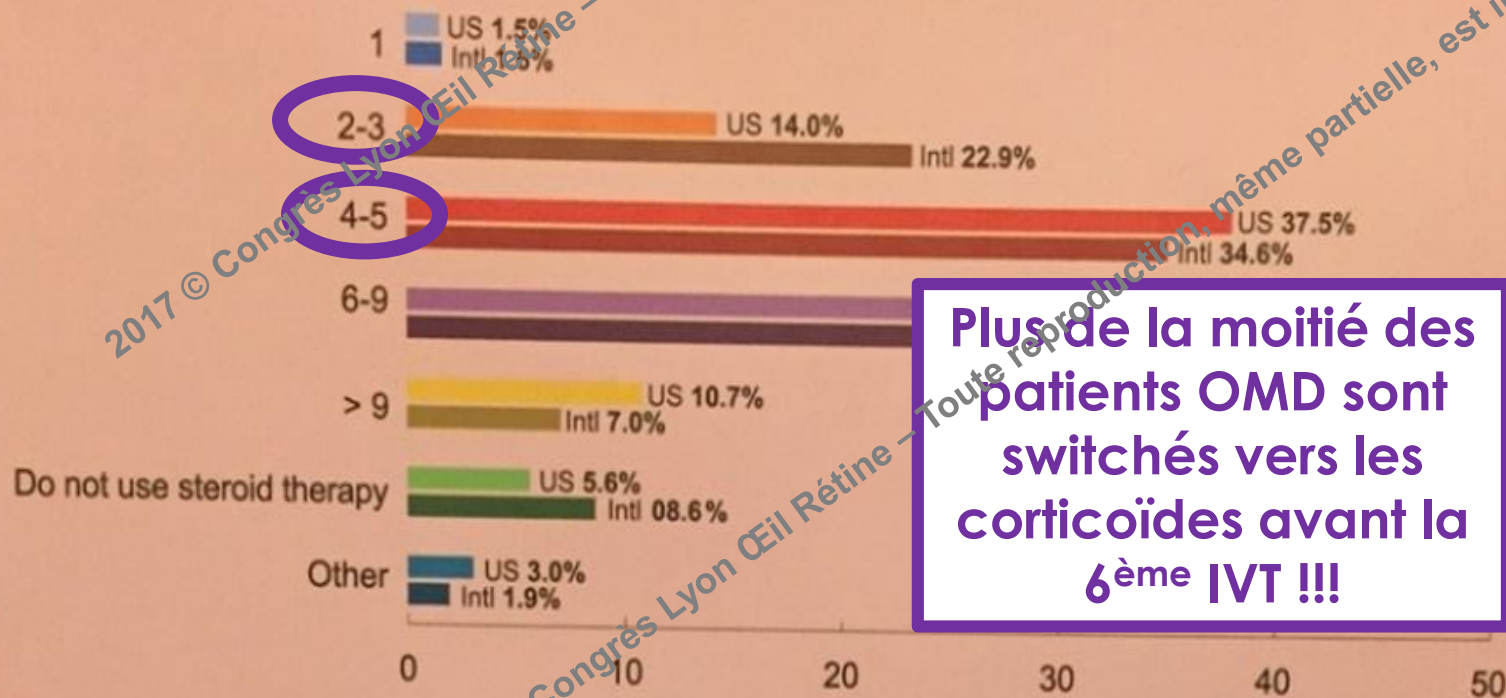
SWITCH VERS DEXA



n°1

Retinal Vascular Diseases/Diabetes

After how many anti-VEGF injections do you consider incorporating steroid therapy?



Plus de la moitié des patients OMD sont switchés vers les corticoïdes avant la 6^{ème} IVT !!!

27. After how many anti-VEGF injections do you consider incorporating steroid therapy?

n = 1070

Pourquoi switcher ?

REVIEW ARTICLE

Diabetic Retinopathy and Diabetic Macular Edema

Pathophysiology, screening, and novel therapies

THOMAS A. CIULLA, MD¹
ARMANDO G. AMADOR, MD²
BERNARD ZINMAN, MD, FRCPC, FACP³

Diabetes Care. 2003 Sep;26(9):2653-64.

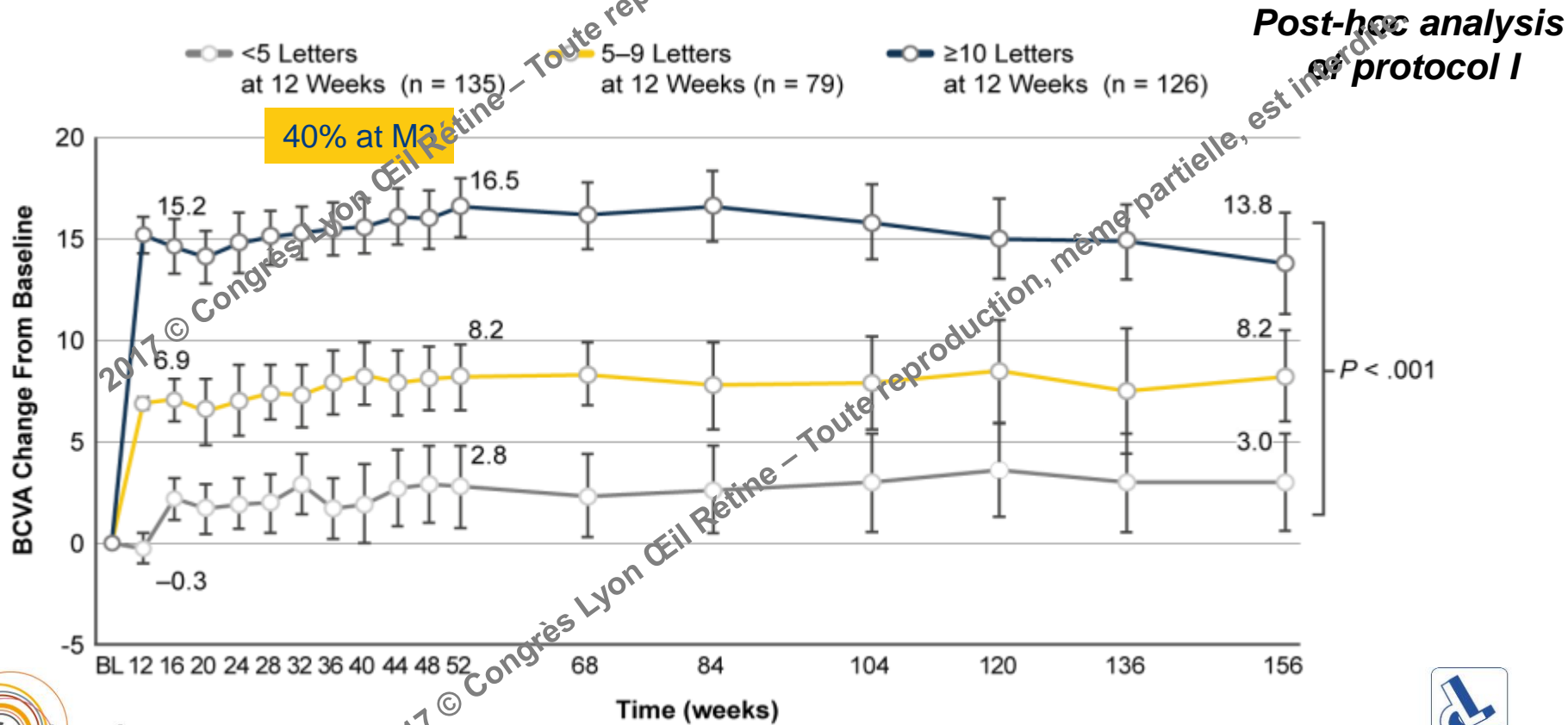
- + de 2 lignes d'AV perdues par > 50% des patients dans les 2 années qui suivent le diagnostic
- Proportion importante de non-répondeur du fait d'une composante inflammatoire importante en cas d'OMD
- L'obstination n'est pas un gage de succès du traitement, au contraire car le retard thérapeutique est une perte de chance

En effet, le pourcentage de non-répondeurs fonctionnels varie peu dans le temps et donc peu dépendant du nombre d'injections !

- **Protocol I:** 28% at 1 year, $\approx 31\%$ at 2 years, $\approx 30\%$ at 3 years
- **Restore (rani 0.5):** 35% at 1 year, 34% at 2 and 3 years
- **Boreal-OMD:** 43% at 3 months, 39% at 6 months, 40% at 1 year
- **Protocol I:** autant d'IVT dans groupe répondeurs et non-répondeurs (fonctionnels et anatomiques, *Bressler et al Arch Ophthalmol 2012*)
- **Luminous OMD naïfs:** AV finale équivalente si 5 à 7 IVT **versus** 8 IVT ou plus

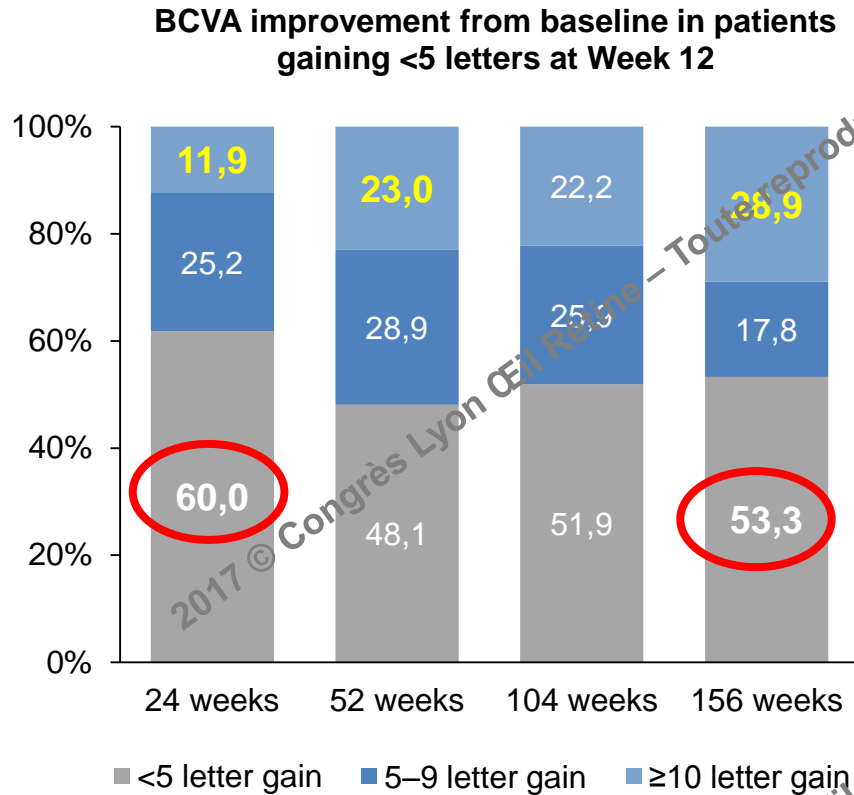
EARLY-STUDY: The relationship between early and long-term responses to ranibizumab

- There is a relationship between early and late treatment response
- 'Poor' initial responders gained approximately 3 letters from baseline at Week 52 and maintained this until Week 156



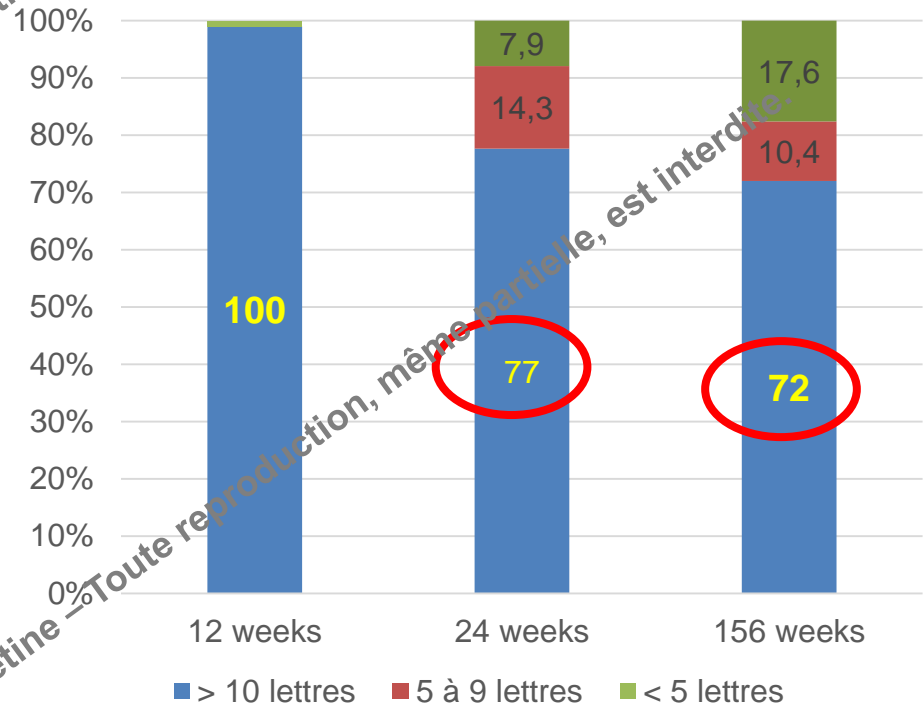
EARLY-STUDY :

Long-term BCVA outcomes in patients gaining <5 letters at Week 12



Patients with a poor initial response may still go on to achieve clinically-significant visual outcomes in the long-term

BCVA improvement from baseline in patients gaining ≥ 10 letters at Week 12



Patients with a good initial response may still present VA impairment in the long-term

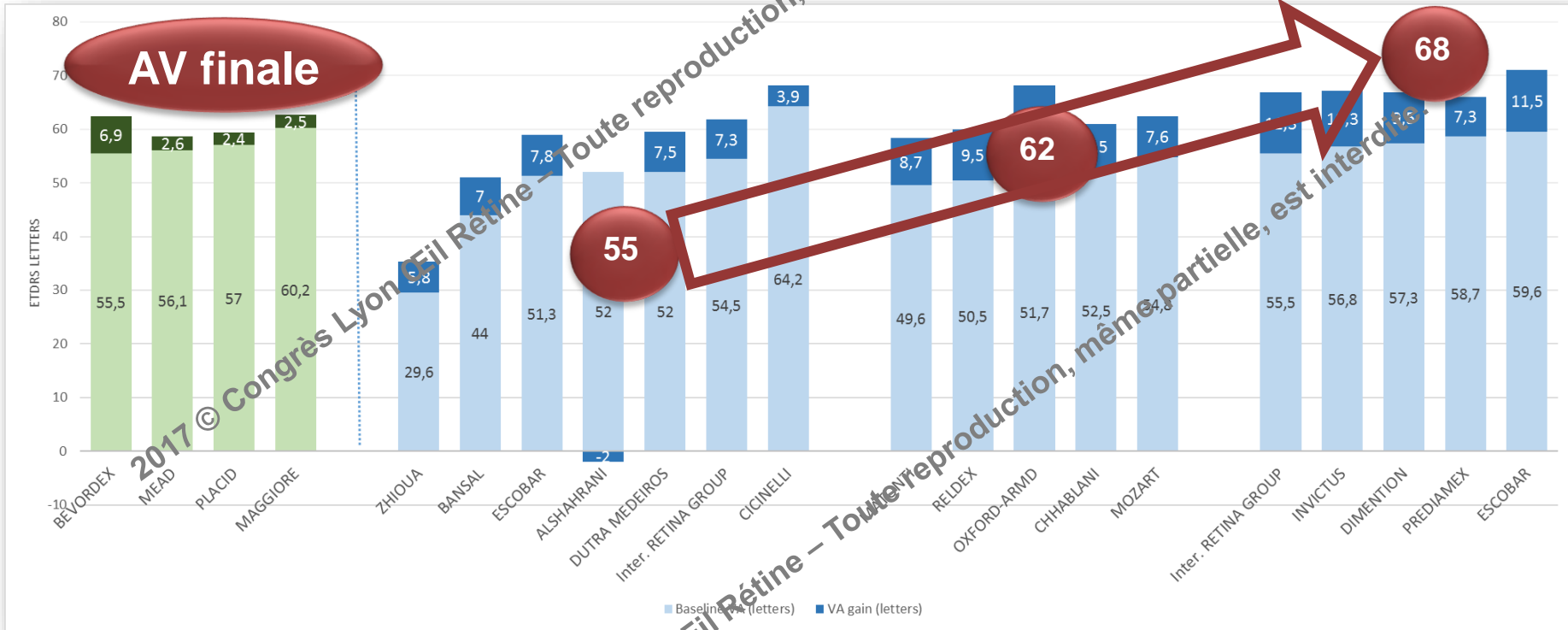


Le secret de bons résultats fonctionnels ...

Traiter précocement !!!!

Ne pas tarder pour switcher ... ou traiter d'emblée même ...

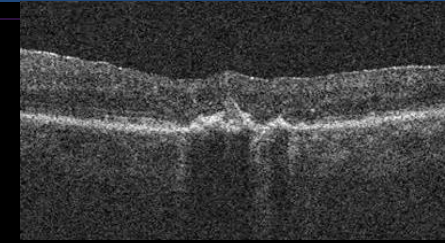
Œdème réfractaire 19 à 50 % naïfs 100% naïfs



Udaondo P et al. Poster PO213 [slide presentation] presented at AAO, New Orleans, USA; 2013.
 Medeiros MD et al. *Ophthalmologica* 2013;231:141-146.
 Escobar-Barranco JJ et al. *Ophthalmologica* 2015;233(3-4):176-85.
 Guigou S et al. *J Fr Ophthalmol* 2014;37:480-485.
 Aknin I et al. *Ophthalmologica* 2016;235(4):187-8.
 Chhablani et al. *Eye (Lond)*. 2016 Mar;30(3):426-30.
 Matonti F et al. *Eur J Ophthalmol*. 2016 Aug 4;26(5):454-9.
 INVICTUS, Matonti F et al. Slides presentation SFO, France; 2017.
 PREDIAMEX, Kodjikian L et al. Slides presentation SFO, France; 2017.
 DIMENSION, Akesbi J et al. Slides presentation SFO, France; 2017
 Malclès A et al. *Retina*. 2017 Apr;37(4):753-760
 Callanan DG et al. *Ophthalmology*. 2013 Sep;120(9):1843-51.
 Callanan DG et al. *Graefes Arch Clin Exp Ophthalmol*. 2017 Mar;255(3):463-473.
 Boyer DS et al. *Ophthalmology*. 2014 Oct;121(10):1904-14.
 Fraser-Bell S et al. *Ophthalmology*. 2016 Jun;123(6):1399-401.

M2 POST IVT DEXA 1

	OG
AV	6/10 Ro1/3
PIO	37 mmHg
SEGMENT ANTÉRIEUR	Calme Pas de rubéose irienne



PRISE EN CHARGE ?

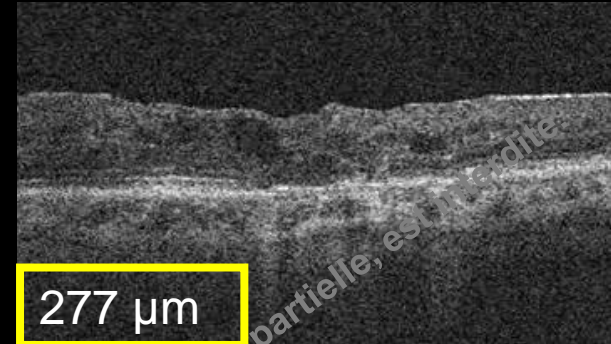
TRAITEMENT LOCAL **BITHERAPIE**
INHIBITEUR ANHYDRASE CARBONIQUE
BÊTABLOQUANT



TRAITEMENT GÉNÉRAL **pour 1 semaine**
ACÉTAZOLAMIDE X 3
CHLORURE DE POTASSIUM X3

M4 POST IVT DEXA 1

	OG
AV	7/10 Ro1/2
PIO	20 mmHg COSOPT
SEGMENT ANTÉRIEUR	Calme Pas de rubéose irienne



Contre indication IVT DEXA?



DEXA & HYPERTONIE

SAFETY OF INTRAVITREAL DEXAMETHASONE IMPLANT (OZURDEX)

The SAFODEX study. Incidence and Risk Factors of Ocular Hypertension

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

Purpose: To analyze the incidence, risk factors, and time course of intraocular pressure elevation after intravitreal dexamethasone implant (Ozurdex).

Methods: The medical charts of 421 consecutive eyes (361 patients) receiving one or more Ozurdex implant between October 2010 and February 2015 were reviewed retrospectively. Ocular hypertension was defined as intraocular pressure of at least 25 mmHg or an increase of at least 10 mmHg from baseline. The main indications for treatment were retinal vein occlusion (34%), diabetic macular edema (30%), postsurgical macular edema (17%), uveitis (14%), and other etiologies (5%).

Results: Among 1,000 intravitreal injections, ocular hypertension was recorded for 28.5% of injected eyes over a mean follow-up period of 16.8 months (3–55). Intraocular pressure-lowering medication was required for 31% of eyes. Only three eyes with preexisting glaucoma required filtering surgery to manage postinjection intraocular pressure elevation. Early retreatment between the third and fourth month does not increase the risk of intraocular pressure elevation. Younger age, male sex, Type 2 diabetes, preexisting glaucoma treated with dual or triple therapy, and a history of retinal vein occlusion or uveitis were significant risk factors for ocular hypertension after dexamethasone implant injection ($P < 0.05$ for all the above).

Conclusion: Episodes of ocular hypertension after Ozurdex implant were generally transient and successfully managed with topical treatment. An analysis of the risk factors may help to determine the risk-benefit ratio for individual patients treated with dexamethasone implants.

RETINA 37:1352–1359, 2017

TOLERANCE OF INTRAVITREAL DEXAMETHASONE IMPLANTS IN PATIENTS WITH OCULAR HYPERTENSION OR OPEN-ANGLE GLAUCOMA

ANNE-LAURE VIÉ, MD,* LAURENT KODJIKIAN, MD, PhD,* ARIANE MALCLÈS, MD,† EMILIE AGARD, MD,† NICOLAS VOIRIN, PhD,‡ HUSSAM EL CHEHAB, MD,† ANH-MINH NGUYEN, MD,* CORINNE DOT, MD, PhD†

Purpose: Evaluate the pressure tolerance of dexamethasone implants in open-angle glaucoma (OAG+) patients and ocular hypertension (OHT+) patients compared with non-glaucomatous and nonhypertensive patients.

Methods: Retrospective observational 2-center, controlled study including 100 patients treated with intravitreal injections of dexamethasone, divided into 2 groups: Group 1, OAG+/OHT+ (n = 50), and Group 2, OAG-/OHT- (n = 50), matched for age and disease. Intraocular pressure (IOP) and hypotensive treatment were evaluated initially, at 8 days, and every month for 6 months after intravitreal treatment. The primary endpoint was IOP increase greater than 10 mmHg.

Results: Thirty-four percent of glaucomatous patients experienced a transient IOP increase greater than 10 mmHg versus 16% in the OAG-/OHT- group ($P = 0.06$). Intraocular pressure greater than 25 mmHg was recorded early on Day 8 in 6% of the OAG+ patients versus 2% of the OAG- patients. Fifty-four percent of the glaucoma patients increased their treatment, and hypotensive treatment was initiated in 38% of the OAG- patients ($P = 0.1$). Filtering surgery was only required in the OAG+/OHT+ group (6% versus 0%), particularly in dual-therapy and triple-therapy patients, who had a higher risk of filtering surgery ($P = 0.008$).

Conclusion: Half of the OAG+ and OHT+ patients needed an add-on treatment, with early onset beginning on Day 8 in 6%. This analysis emphasizes the need for IOP monitoring during treatment, especially for OAG+/OHT+ patients.

RETINA 37:173–178, 2017

Intraocular Dexamethasone Implant Position *in situ* and Ocular Hypertension
Sudhakar Kodjikian et al
Accepted in Retina

2017

Evaluation of efficacy and safety of dexamethasone intravitreal implants before and after vitrectomy in a real-life study
Rezkallah, Kodjikian et al
Accepted in Acta Ophthalmologica
2017



Graefes Arch Clin Exp Ophthalmol
DOI 10.1007/s00417-017-3773-z

LETTER TO THE EDITOR

DEX implant intravitreal injection, sustained intraocular hypertension, and steroid-induced glaucoma in patients with no risk factors

Rezkallah Amina¹ • Kodjikian Laurent¹ • Malclès Ariane¹ • Dot Corinne^{2,3}



Est-ce-que l'HTIO est fréquente ?

- 421 yeux – 1000 DEXA – toutes indications
 - 28,5% ont PIO \geq 25 mmHg et/ou gain \geq 10 mmHg
 - 20% de PIO \geq 25 mmHg
- Prévalence varie selon les indications
 - Risque le plus faible statistiquement pour OMD (/r OVR & uvéites)
 - 11% de PIO \geq 25 mmHg
 - 3% de hauts-répondeurs (gain > 15 mmHg)
- Prévalence varie selon le statut glaucomateux
 - HTIO à baseline : 0% de hauts-répondeurs
 - GCAO sous monothérapie à baseline : 5% de hauts-répondeurs
 - Sous bi- ou tri-thérapie : 50 à 100% de hauts-répondeurs !!!

SAFETY OF INTRAVITREAL DEXAMETHASONE IMPLANT (OZURDEX) The SAFODEX study. Incidence and Risk Factors of Ocular Hypertension

ARIANE MALCÈS, MD,* CORINNE DOT, MD, PhD,†† NICOLAS VOIRIN, PhD,* ANNE-LAURE VIE, MD,* ÉMILIE AGARD, MD,†† DAVID BELLOCO, MD,* PHILIPPE DENIS, MD, PhD,* LAURENT KODJIKIAN, MD, PhD*

Purpose: To analyze the incidence, risk factors, and time course of intracocular pressure elevation after intravitreal dexamethasone implant (Ozurdex).

Methods: The medical charts of 421 consecutive eyes (261 patients) receiving one or more Ozurdex implant between October 2010 and February 2015 were reviewed retrospectively. Ocular hypertension was defined as intracocular pressure of at least 25 mmHg or an increase of at least 10 mmHg from baseline. The main indications for treatment were retinal vein occlusion (34%), diabetic macular edema (30%), postoperative macular edema (17%), uveitis (14%), and other etiologies (5%).

Results: Among 1,000 intravitreal injections, ocular hypertension was recorded for 28.5% of injected eyes over a mean follow-up of 18 months (9-55). Intracocular pressure-lowering medication was required for 10.5% of eyes. Only three eyes with preexisting glaucoma required filtering surgery to resolve elevated intracocular pressure elevation. Early treatment between the first and fourth month does not increase the risk of intracocular pressure elevation. Younger age, male sex, and 1 diabetes, preexisting glaucoma treated with dual or triple therapy, and a higher baseline were not significant risk factors for ocular hypertension after dexamethasone implant injection (P < 0.05 for all the above).

Conclusions: The risk of ocular hypertension after Ozurdex implant were generally transient and usually managed with topical treatment. An analysis of the risk factors may help to determine the risk-benefit ratio for individual patients treated with dexamethasone implants.

DOI: 10.1093/ptj/ptj1352-1359, 2017

Recommandations SFO/SFG 2017

Est-ce-que l'HTIO est facilement contrôlable ?

- Parmi nos 120 cas d'hypertonie
 - Besoin d'ajouter un hypotonisant : 1/3
 - 97% de ces patients ont été contrôlés par un traitement topique
 - 0,7% de chirurgie filtrante
- **Peut-on ré-injecter un patient qui a présente une HTIO sous DEXA ?**
 - **OUI**, si HTIO contrôlée **et** patient faible ou moyen répondeur (gain PIO \leq 15 mmHg)
 - Alors prescrire un ttt topique prophylactique identique au ttt initial pour une durée de 3 mois post-IVT

SAFETY OF INTRAVITREAL DEXAMETHASONE IMPLANT (OZURDEX)

The SAFODEX study. Incidence and Risk Factors of Ocular Hypertension

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

Purpose: To analyze the incidence, risk factors, and time course of intraocular pressure elevation after intravitreal dexamethasone implant (Ozurdex).

Methods: The medical charts of 421 consecutive eyes (92 patients) receiving one or more Ozurdex implant between October 2010 and February 2011 were reviewed retrospectively. Ocular hypertension was defined as intraocular pressure of at least 25 mmHg or an increase of at least 10 mmHg from baseline. The main indications for treatment were retinal vein occlusion (34%), diabetic macular edema (39%), postsurgical macular edema (17%), uveitis (14%), and other etiologies (5%).

Results: Among 1,000 intravitreal injections, ocular hypertension was recorded for 28.5% of injected eyes over a mean follow-up period of 16.8 months (3–55). Intraocular pressure-lowering medication was required in 13% of eyes. Only three eyes with preexisting glaucoma required filtering surgery to prevent postinjection intraocular pressure elevation. Early retreatment between the third and sixth month does not increase the risk of intraocular pressure elevation. Younger age, male sex, Type 1 diabetes, preexisting glaucoma treated with dual or triple therapy, and history of retinal vein occlusion or uveitis were significant risk factors for ocular hypertension after dexamethasone implant injection ($P < 0.05$ for all the above).

Conclusion: Episodes of ocular hypertension after Ozurdex implant were generally transient and successfully managed with topical treatment. An analysis of the risk factors may help to determine the risk-benefit ratio for individual patients treated with dexamethasone implants.

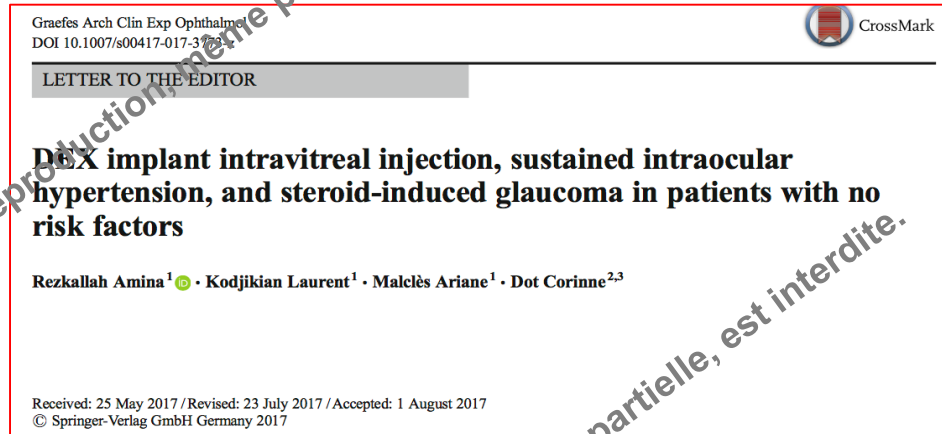
RETINA 37:1352–1359, 2017

Recommandations SFO/SFG 2017

Est ce que l'HTIO est persistante **et** existe t-il un risque de glaucome cortisoné ?

- **NON avec DEXA**

*HTIO transitoire, sans
risque de glaucome
cortisoné*



- **Différent de la triamcinolone et de l'iluvien**

- Fitzgerald et al Clin Exp Ophthalmol. 2015 Apr;43(3):234-8
- Kiddee et al Surv Ophthalmol 2013; 58: 291–310
- Campochiaro et al Ophthalmology. 2011 Apr;118(4):626-635

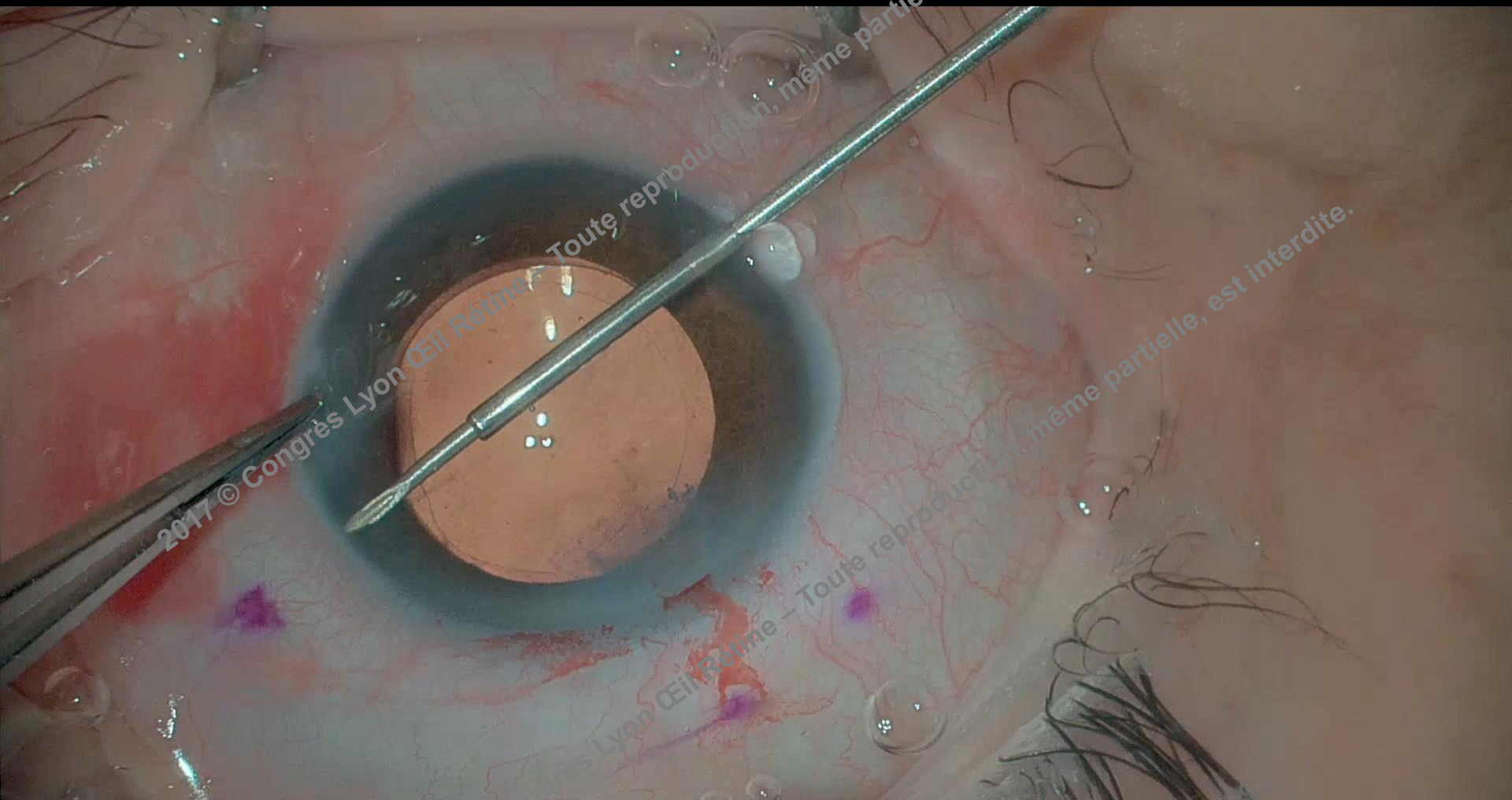
M1 POST IVT DEXA 2

PIO	32 mmHg
Traitement	<u>Bithérapie</u> <u>COSOPT</u>



INTOLÉRANCE DIAMOX + diabète !

PRISE EN CHARGE ?



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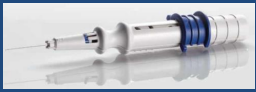
J8 XEN



	OG
AV	6/10 Ro1/3
PIO	6 mmHg
SEGMENT ANTERIEUR	BDF+ XEN en place CA formée

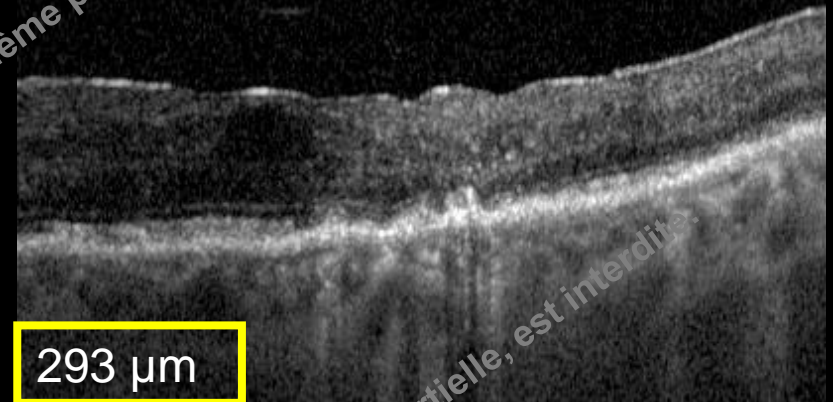


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J15 XEN // M3 DEXA 2

	OG
AV	6/10 Ro1/3
PIO	6 mmHg
SEGMENT ANTÉRIEUR	BDF+ XEN en place CA formée Pas de DC



NOUVELLE DEXA ?

OUI !



n°3

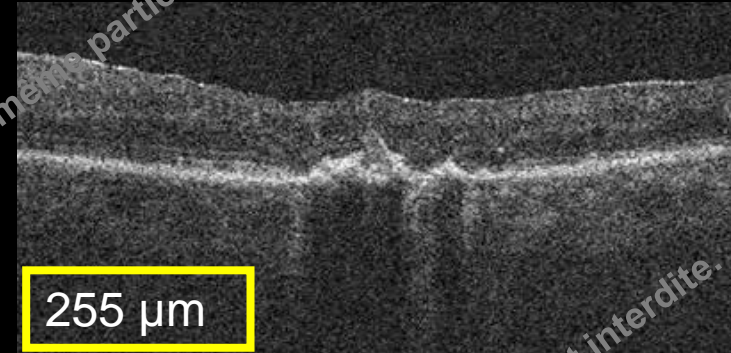
J21 XEN // J8 DEXA 3

	OG
AV	5/10 Ro1/4
PIO	8 mmHg
SEGMENT ANTÉRIEUR	Calme BDF+ XEN en place



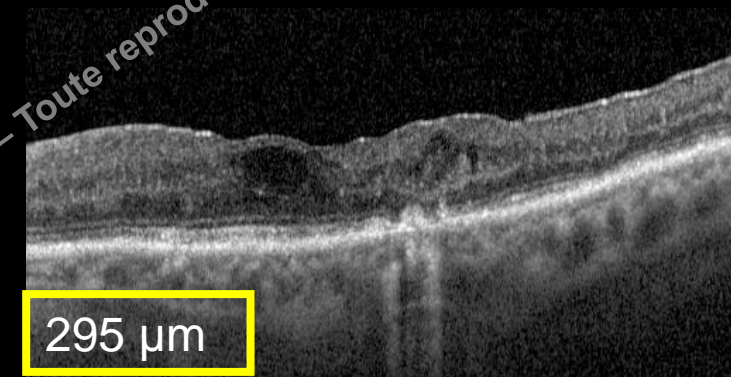
M2,5 XEN // M2 DEXA 3

	OG
AV	6/10 Ro1/3
PIO	9 mmHg
SEGMENT ANTÉRIEUR	BDF+ XEN en place CA formée



M4,5 XEN // M4 DEXA 3

	OG
AV	6/10 Ro1/3
PIO	7 mmHg
SEGMENT ANTÉRIEUR	BDF+ XEN en place CA formée



n°4

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À SUIVRE ...

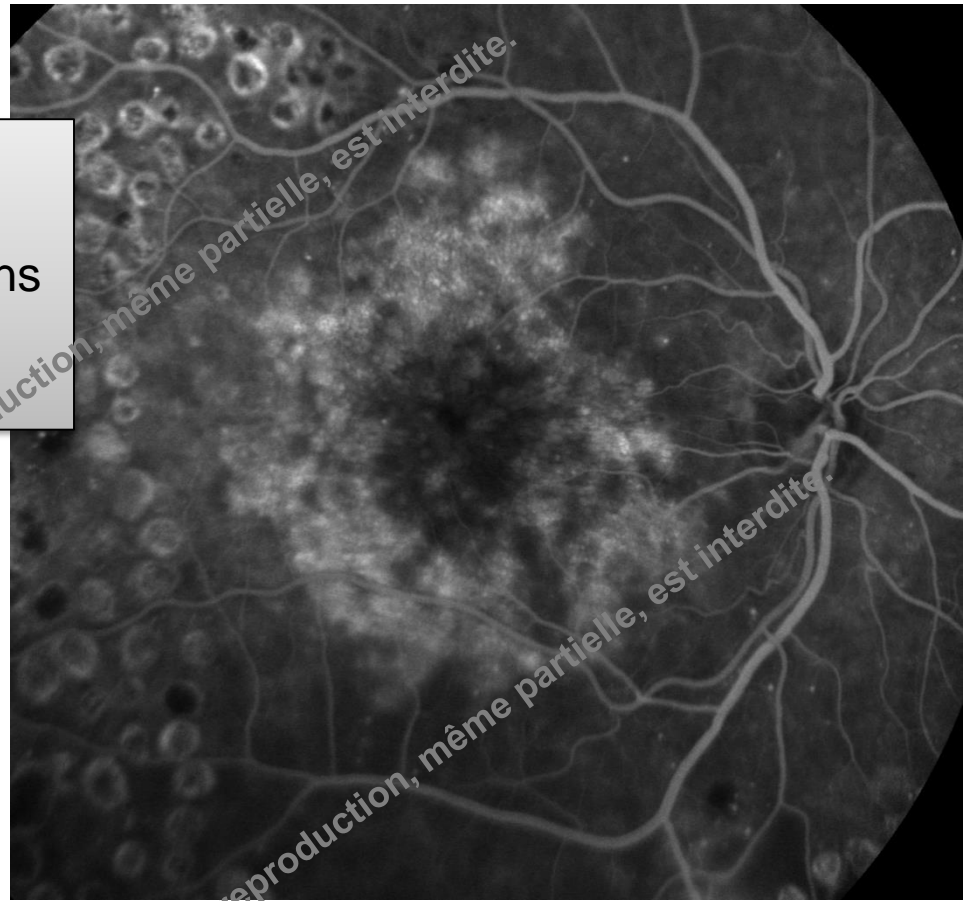
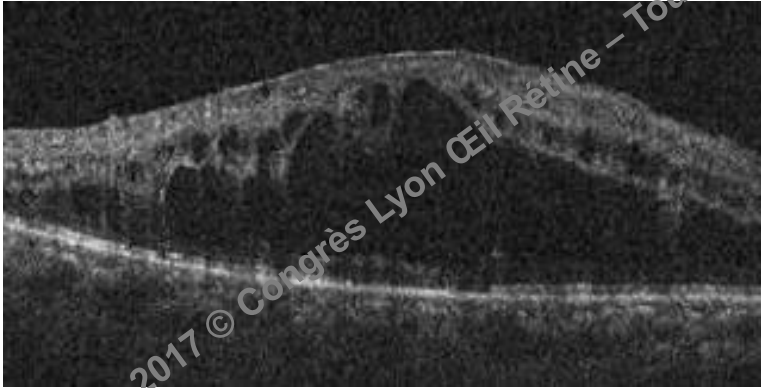
2017 © Congrès Lyon Œil Rétine – Toute reproduction, même partielle, est interdite.



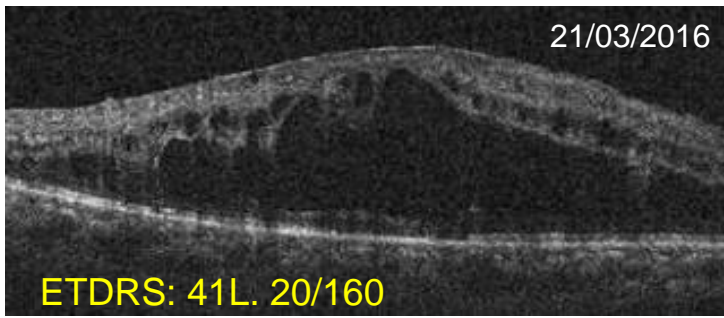
M.A

- Patient de 52 ans
- Diabète de type 2 depuis 12 ans
- HbA1c 8,1%
- HTA bien équilibrée
 - Phaque ODG
 - Antécédents de PRP ODG
- Suivi ophtalmologique peu régulier, dernière consultation il y a plus de 3 ans

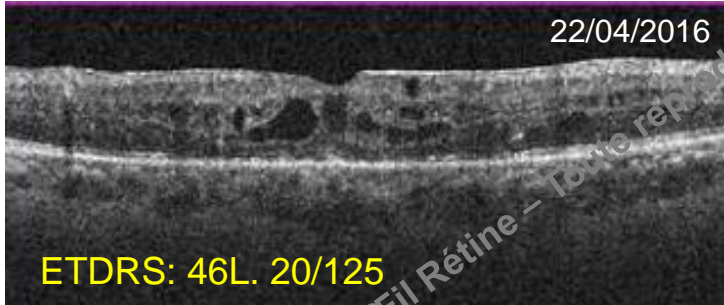
AV OD 41Le ETDRS
PRP complète ODG
OMC important avec EMC 743 microns
Pas d'antécédent d'IVT



→ Indication IVT anti-VEGF chez un patient jeune, phake avec cristallin clair



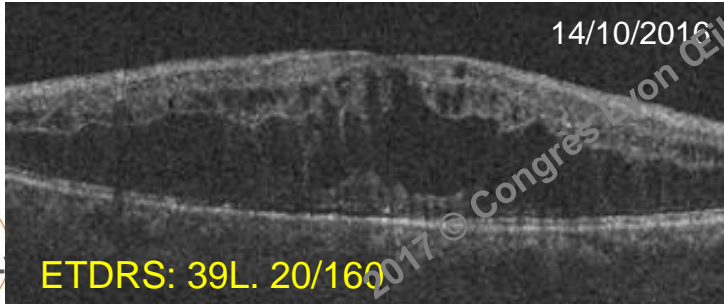
ranibizumab n° 1



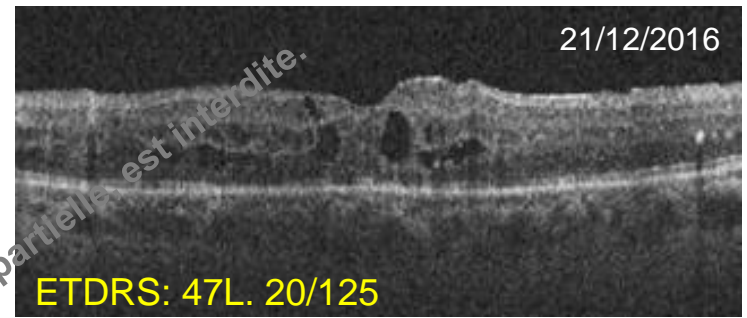
ranibizumab n° 2



ranibizumab n° 3

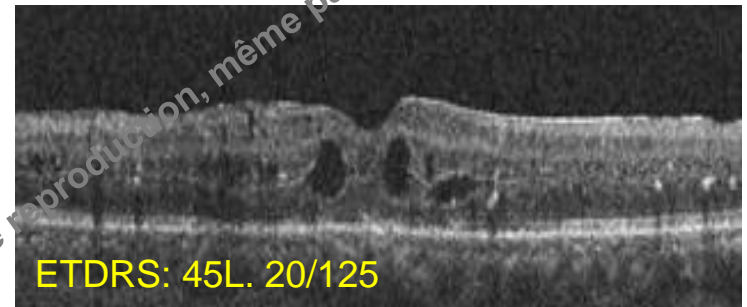


ranibizumab n° 4



ranibizumab n° 5

Nouvelle consultation le 03/03/2017



✓ 5 IVT ranibizumab la 1^{ère} année

(suivi irrégulier)

✓ **GAIN DE +4 lettres**



Diabetic Macular Edema Diagnosis and Treatment in the Real World: An Analysis of Medicare Claims Data (2008 to 2010)

Pravin U. Dugel, MD; Andrew Layton, BA; Rohit Varma, MD, MPH

[*Ophthalmic Surg Lasers Imaging Retina*. 2016;49:258-267.]

Patients without anti-VEGF treatment for DME 1 year prior to first anti-VEGF treatment in 2008-2010 N = 772		
2008 n = 101	2009 n = 249	2010 n = 422

- Retrospective « Medicare » study of naïve DME patients treated with anti-VEGF
- **Mean number of IVI: 4.2** (3.1 to 4.6)
- 19% had additional triamcinolone IVI, 34% additional laser
- 65% of patients stopped anti-VEGF during the 1st year of treatment

TABLE 3
DME Treatment Frequency Based on Number of Claims per Patient

	Patients, n	Claims, n	Patients With Claim Submitted, n	Mean Claims Per Patient With Service
Services for DME	772	6,654	100	8.6
Anti-VEGF Treatment for DME ^a	772	3,220	100	4.2
IVTA Treatment for DME ^a	149	363	19	2.4
Focal Laser Services for DME ^a	260	611	34	2.4

* IVTA is not indicated for DME treatment

Trends in the Care of Diabetic Macular Edema: Analysis of a National Cohort

Brian L. VanderBeek^{1,2,3*}, Neepa Shah¹, Purak C. Parikh¹, Livuan Ma³

Design

Retrospective cohort study.

2 years of follow-up

Methods

Setting: Administrative medical claims data from a large, national U.S. insurer. **Study population:** Beneficiaries of a U.S. insurance company. **Observation procedures:** All incident

Table 3. 2-year cohort data on treatment types and frequencies

	2002/3–2005	2006–8	2010–12	p-value
Patients (PT)	233	251	756	
Total Office Visits	787	838	2853	
Focal Laser Treatments				
% PT w/ focal laser (N)	22.75% (53)	35.06% (88)	36.64% (277)	<0.001
Total focal lasers performed	68	158	552	
Range of focals performed	0–4	0–10	0–10	
# Focals/focal PT (SD)	1.28 (0.63)	1.80 (1.39)	1.99 (1.44)	<0.001
# Focals/total visits (SD)	8.64% (0.28)	18.85% (0.39)	19.34% (0.40)	<0.001
Anti-VEGF Treatments				
% PT w/ Anti-VEGF (N)	0% (0)	2.00% (5)	14.55% (110)	<0.001
Total Anti-VEGF injections	0	10	430	
Range of injections performed	0	0	0–15	
# Injections/anti-VEGF PT (SD)	0 (NA)	2.00 (1.00)	3.91 (3.21)	0.19
# Injections/total visits (SD)	0 (NA)	1.19% (0.11)	15.07% (0.36)	<0.001
Steroid Injections				
% PT w/ steroid (N)	0% (0)	1.20% (3)	2.38% (18)	0.04
Total steroid injections	0	3	31	
Range of injections performed	0	0–1	0–5	
# Injections/steroid PT (SD)	0 (NA)	1 (0.00)	1.72 (1.18)	0.31
# Injections/total visits (SD)	0 (NA)	0.36% (0.06)	1.09% (0.10)	0.003
Any Treatment				
% PT with any treatment (N)	22.75% (53)	35.86% (90)	40.48% (306)	<0.001

doi:10.1371/journal.pone.0149450.t003

Results

Two-year cohorts had 233, 251 and 756 patients in 2002/3, 2006 and 2010 respectively. One-year cohorts had 1002, 1119 and 1332 patients in 2009, 2010 and 2011, respectively. Both percentage of patients receiving therapy and number of treatments given increased across the 2-year cohorts for both focal laser and anti-vascular endothelial growth factor (anti-VEGF) ($p < 0.001$). The highest use of anti-VEGF agents in any of the cohorts was in the 2011 1-year group that only averaged 3.78 injections. Focal laser was used 2.5x as frequently as anti-VEGF injections in the most recent cohorts with only a high of 14.0% of DME patients receiving anti-VEGF therapy in any of the cohorts.

Conclusion

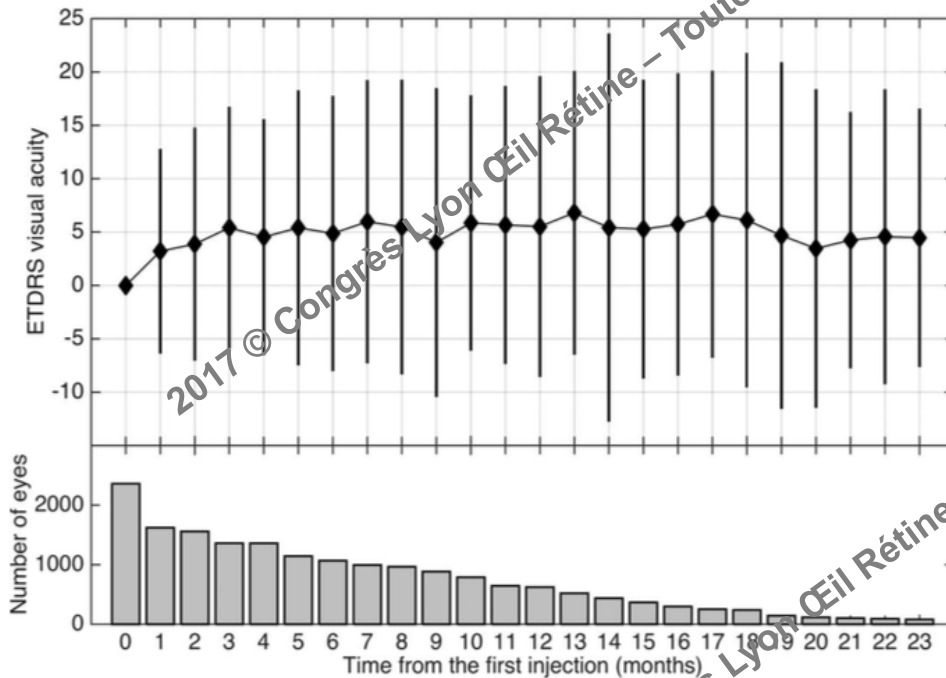
Regardless of treatment modality (laser or injection) DME patients received vastly fewer treatments than patients in randomized control trials. Despite the proven superior visual



LONG TERM EFFICACY OF ANTI-VEGF: 2 YEARS

The United Kingdom Diabetic Retinopathy Electronic Medical Record Users Group, Report 1: baseline characteristics and visual acuity outcomes in eyes treated with intravitreal injections of ranibizumab for diabetic macular oedema

Egan C, et al. Br J Ophthalmol 2017;101:75–80



19 UK centres
Data from 12989 clinic visits about
3103 DME eyes

Follow-up of 2 years

Mean visual gain : 5 letters

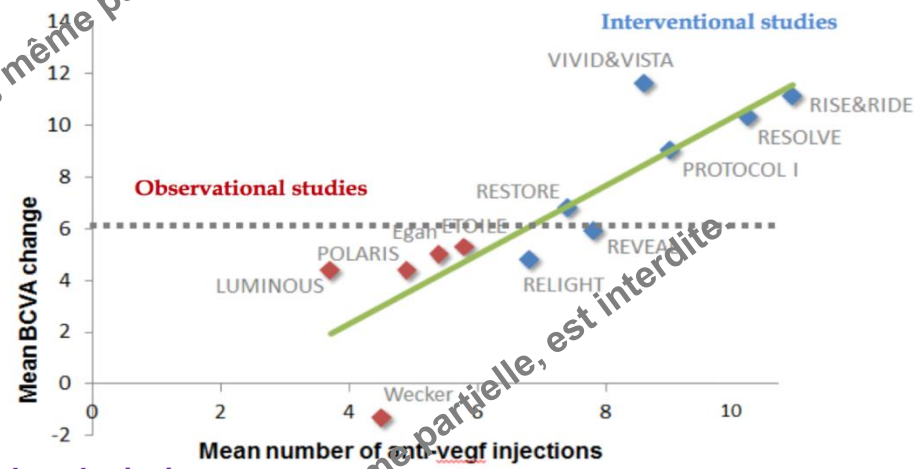
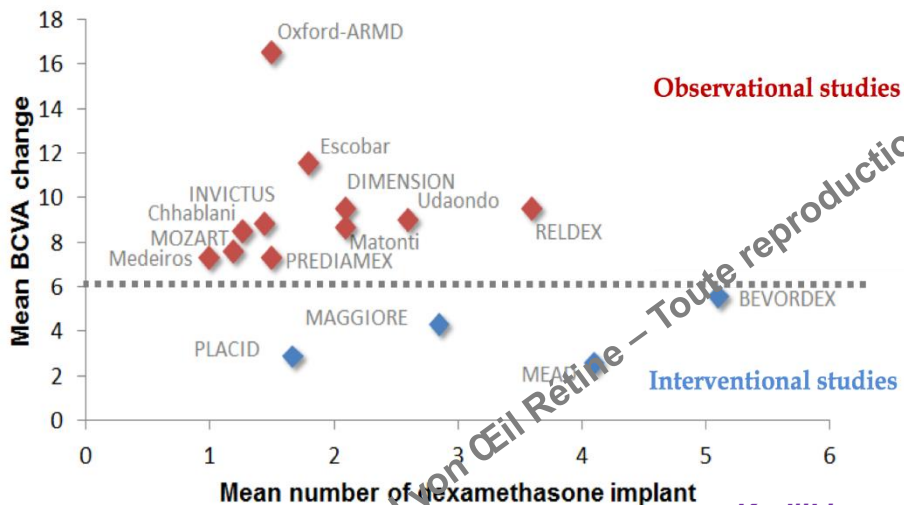
Mean of 3.3 injections the 1st year

For the eyes followed at least 2 years

Baseline VA: 51.1 (SD 19.3) letters

1-year VA: 54.2 (SD 18.6) letters

Real Life **versus** RCTs Visual Outcomes



Kodjikian et al. In submission

Real life of DEX implant shows **better outcomes** than both DEX RCT and Real life Anti-VEGF (RBZ)

BIG difference between RCT and Real life (RBZ) mainly due to the tight schedule of injections - mandatory to achieve best outcomes

Udaondo P et al. Poster PO213 [slide presentation] presented at AAO, New Orleans, USA; 2017.
 Medeiros MD et al. *Ophthalmologica* 2013;231:141-146.
 Escobar-Barranco JJ et al. *Ophthalmologica* 2015;233(3-4):176-85.
 Guigou S et al. *J Fr Ophthalmol* 2014;37:480-485.
 Aknin I et al. *Ophthalmologica* 2016;235(4):187-8.
 Chhablani et al. *Eye (Lond)*. 2016 Mar;30(3):426-30.
 Matonti F et al. *Eur J Ophthalmol*. 2016 Aug 4;26(5):454-9.
 INVICTUS, Matonti F et al. Slides presentation SFO, France; 2017.

PREDIAMEX, Kodjikian L et al. Slides presentation SFO, France; 2017.
 DIMENSION, Akesbi J et al. Slides presentation SFO, France; 2017
 Malclès A et al. *Retina*. 2017 Apr;37(4):753-760
 Callanan DG et al. *Ophthalmology*. 2013 Sep;120(9):1843-51.
 Callanan DG et al. *Graefes Arch Clin Exp Ophthalmol*. 2017 Mar;255(3):463-473.
 Boyer DS et al. *Ophthalmology*. 2014 Oct;121(10):1904-14.
 Fraser-Bell S et al. *Ophthalmology*. 2016 Jun;123(6):1399-401.
 Adapté de Kiss S et al. *Clin Ophthalmol*. 2014 Aug 26;8:1611-21.

⑩ Mme B âgée de 65 ans, DNID depuis 13 ans

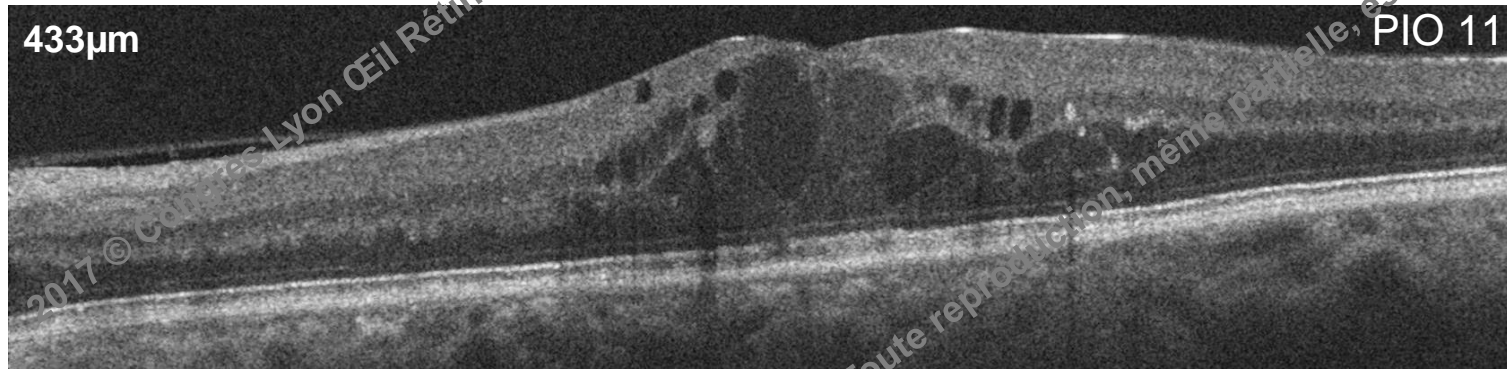
☞ HbA1c = 7,6%, TA équilibrée

☞ AV OD = 4/10 P4

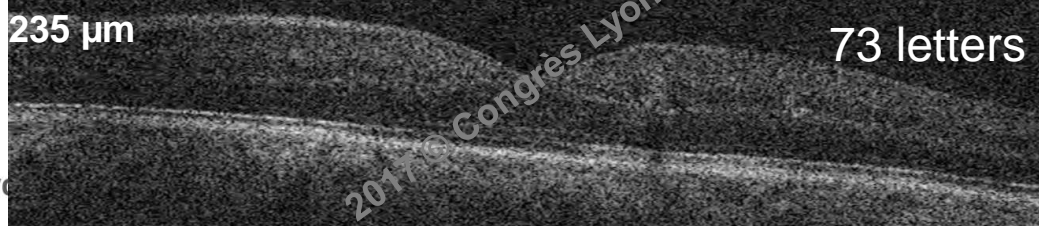
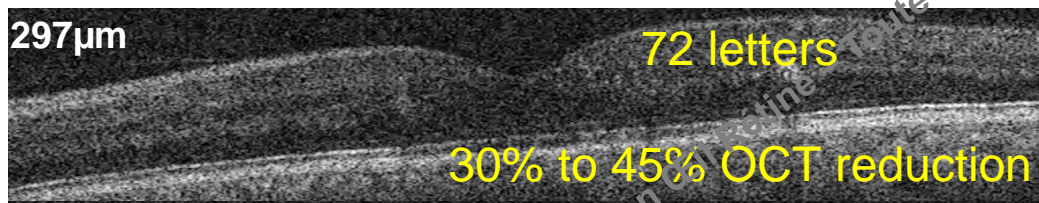
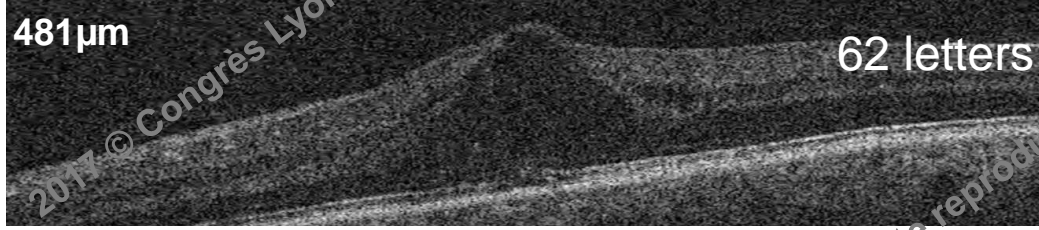
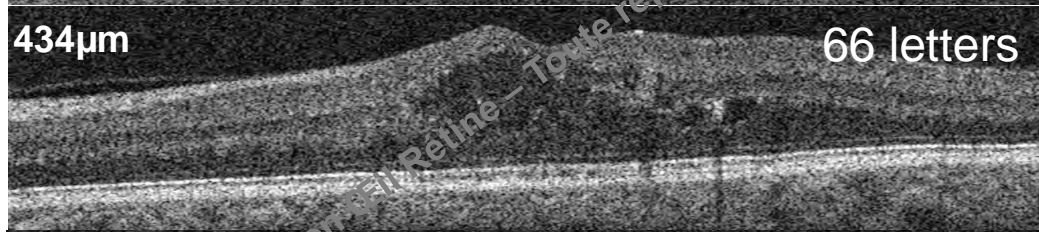
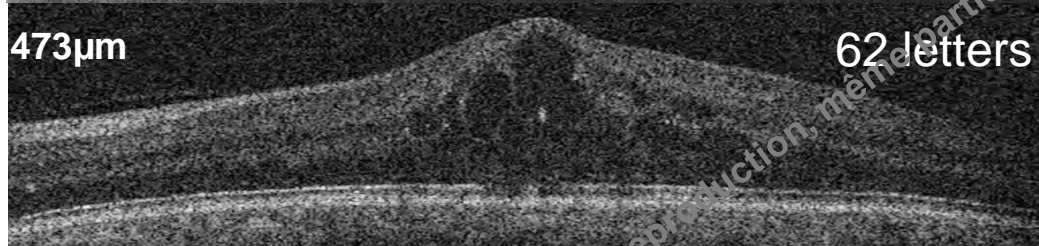
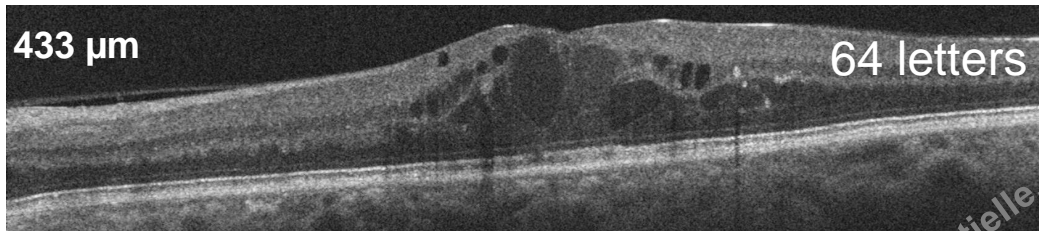
☞ Phake

☞ FO: RDNP modérée ODG

☞ OCT



Indication IVT anti-VEGF (ranibizumab) x 3 OG



est interdite.

IVT N°1 ranibizumab

M+1 IVT n°1 ranibizumab

IVT N°2 ranibizumab

M+1 IVT n°2 ranibizumab

IVT N°3 ranibizumab

M+1 IVT n°3 ranibizumab

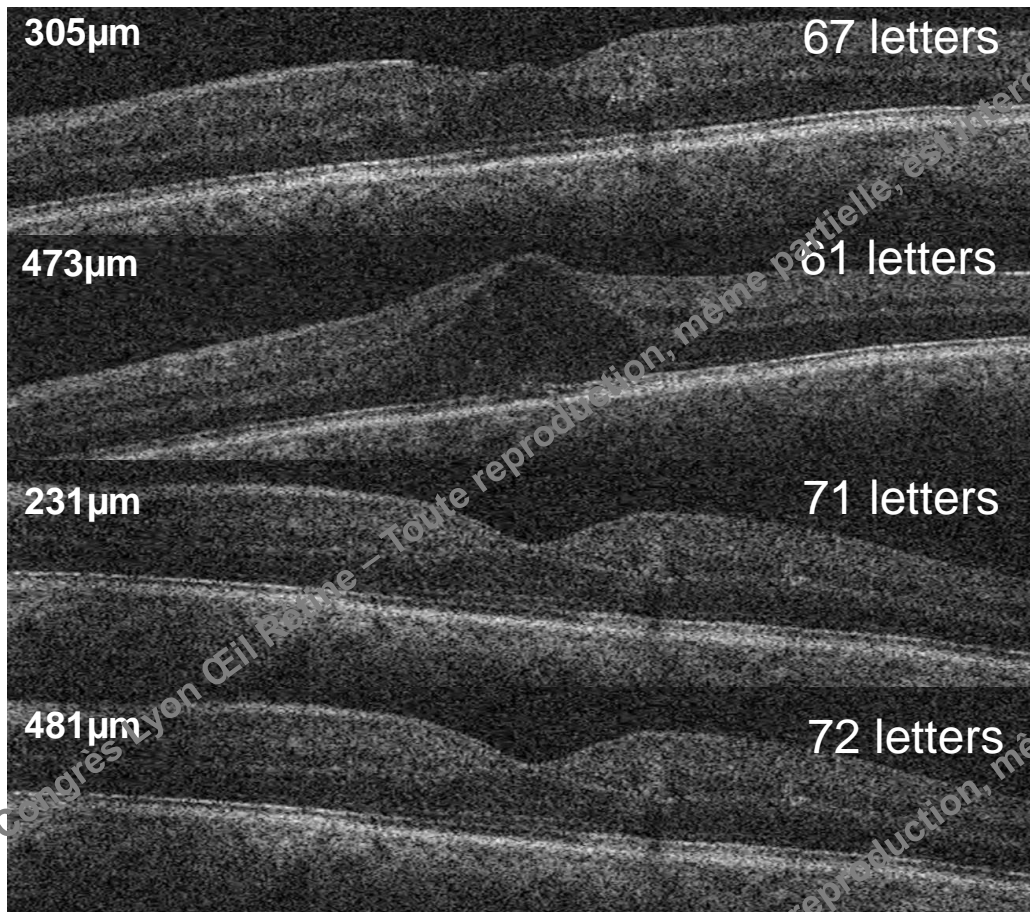
switch précoce vers DEXA
car pas eff. fonctionnelle (gain < 5 lettres) ni anatomique (↓ < 20%)

M+1 IVT n°1 DEXA

M+2 IVT n°1 DEXA

30% to 45% OCT reduction





M+4 IVT n°1 DEXA

M+6 IVT n°1 DEXA

IVT N°2 DEXA

M+2 IVT n°2 DEXA

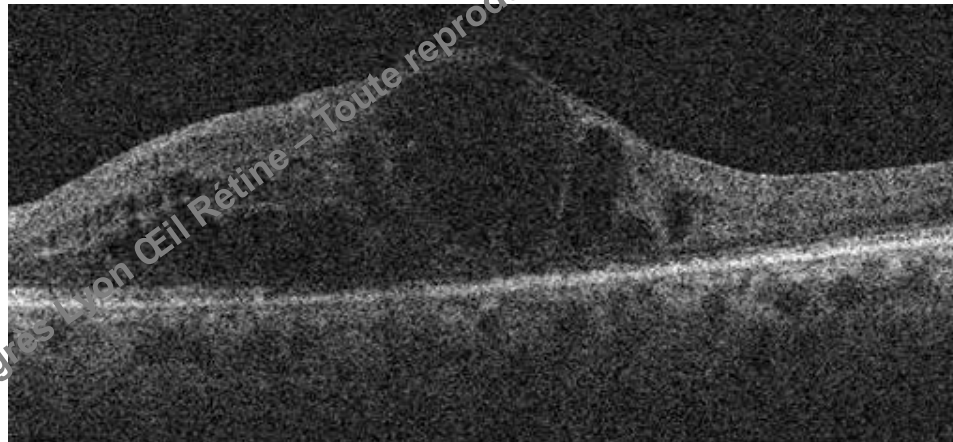
M+4 IVT n°2 DEXA

**Pas encore d'aggravation
de la cataracte**

- Phake de 75 ans
- Non-répondeur fonctionnel ni anatomique au ranibizumab
- Switch précoce à M4 vers DEXA, avec cette fois une réponse anatomique (diminution de 45% de l'épaisseur) **et** fonctionnelle (gain de 8 à 9 lettres)

OMD

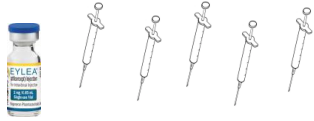
- Madame A. 78 ans
- HbA1c 7,8%
- RDNP sévère aux deux yeux
- AV ETDRS 60 lettres OG



60 lettres

J0

370 µm



60 lettres

M1

270 µm

Répondeur anatomique seulement



60 lettres

M1

285 µm



n°7

M1

59 lettres

283 µm

M2

60 lettres

285 µm



n°9

M1

60 lettres
Pas d'amélioration

300 µm



n°8

M1

62 lettres

278 µm

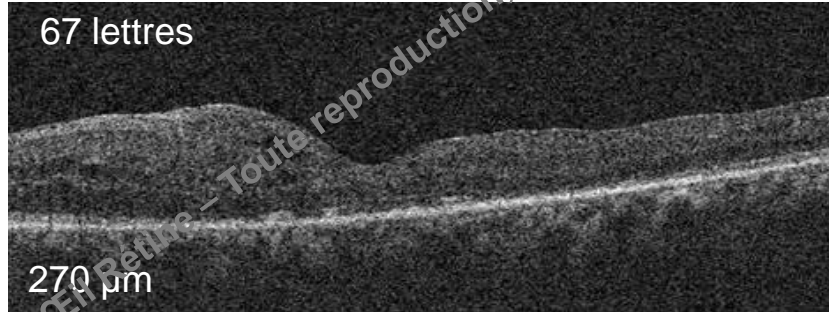
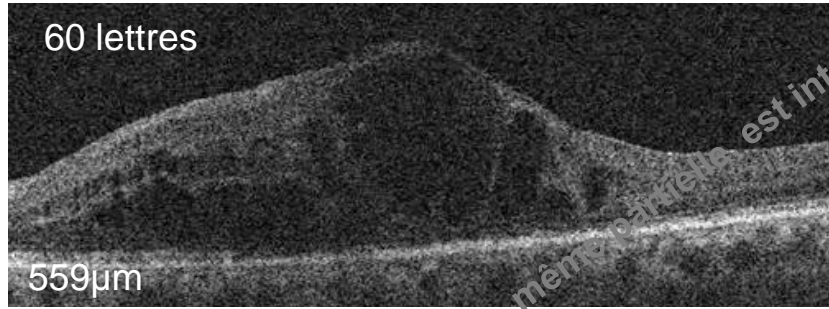
STOP aflibercept

SWITCH DEXA

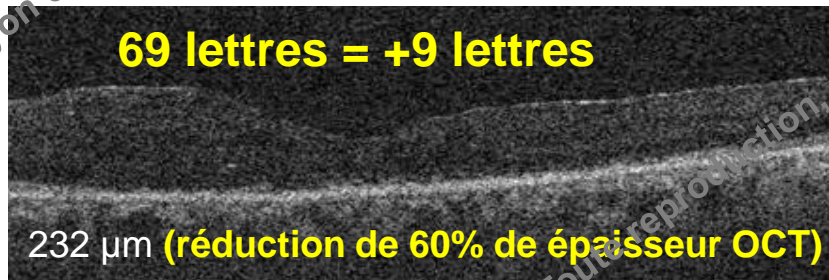




M1 DEXA



M2 DEXA



M4 DEXA



Bonne réponse
fonctionnelle et
anatomique

et moins
d'injections !