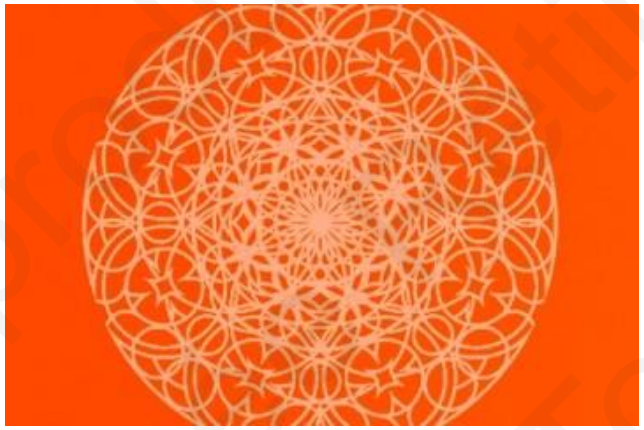
4e Journée Rétine et Diabète



29 novembre 2024

Risque inflammatoire lié aux nouveaux anti-VEGF

Pr. Pierre-Henry Gabrielle MD PhD FEBO
Service d'ophtalmologie du CHU DIJON, Dijon
Fight Retinal Blindness! registry, Save Sight Institute, Sydney

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Save Sight Registries
Seeing Outcomes

SAVE SIGHT INSTITUTE

CHU Centre Hospitalier Universitaire Dijon Bourgogne

UB UNIVERSITÉ DE BOURGOGNE

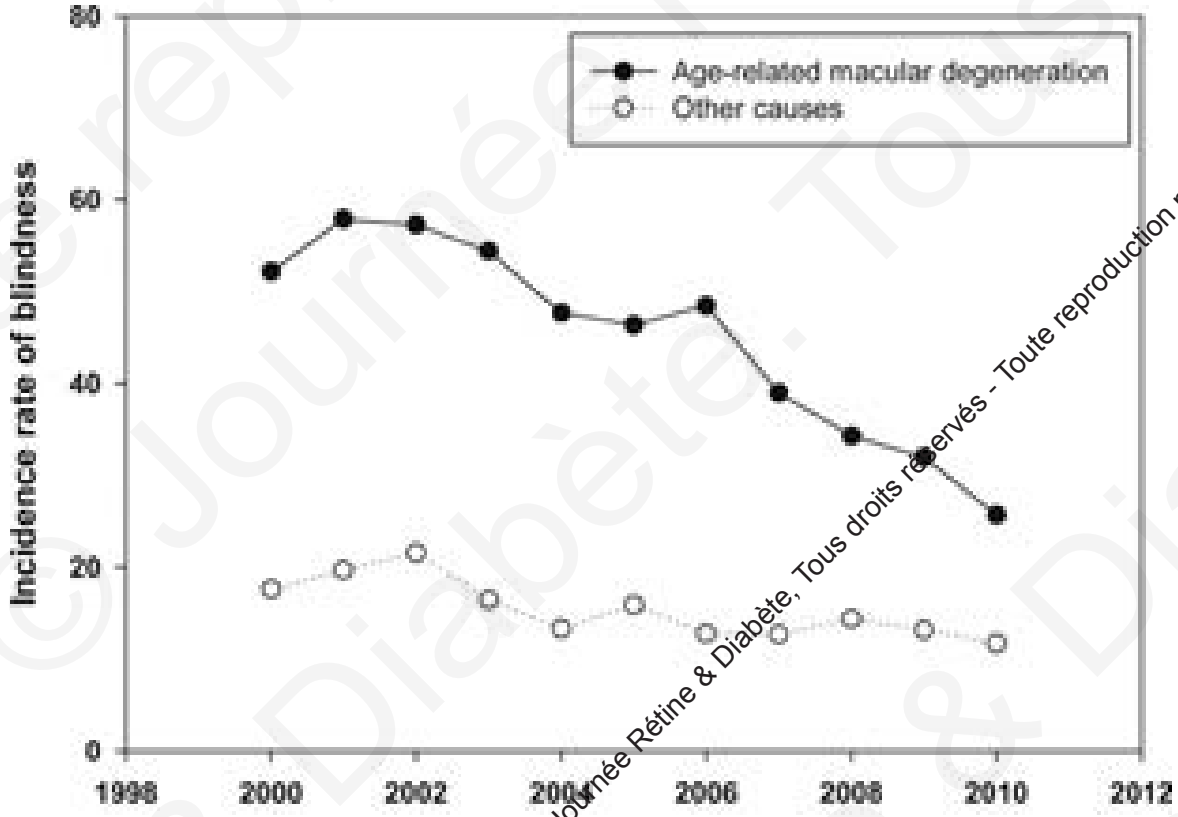
Conflits d'intérêts

Consultant : **Novartis**, **Bayer**, **Roche**, Astellas, Horus et Zeiss

Frais de voyage pour des congrès : Allergan/Abbvie, **Roche**, Horus, **Novartis et Bayer**

Introduction

Les anti-VEGF ont révolutionné la prise en charge des maladies rétiniennes



Risque inflammation oculaire (IO)
AVANT les nouvelles molécules d'anti-VEGF

ORIGINAL ARTICLE

Ranibizumab for Neovascular Age-Related Macular Degeneration

Authors: Philip J. Rosenfeld, M.D., Ph.D., David M. Brown, M.D., Jeffrey S. Heier, M.D., David S. Boyer, M.D., Peter K. Kaiser, M.D., Carol Y. Chung, Ph.D., and Robert Y. Kim, M.D., for the MARINA Study Group* Author Info & Affiliations

Published October 5, 2006 | N Engl J Med 2006;355:1419-1431 | DOI: 10.1056/NEJMoa054481 | VOL 355 NO. 14

Table 2. Adverse Events at 24 Months.*

Adverse Event	Sham Injection (N=236)	0.3 mg of Ranibizumab (N=238)	0.5 mg of Ranibizumab (N=239)
Serious ocular event — no. (%)			
Presumed endophthalmitis†	1	2 (0.8)	3 (1.3)
Culture not obtained	0	1 (0.4)	0
Culture negative	0	1 (0.4)	3 (1.3)‡
Uveitis	0	3 (1.3)	3 (1.3)§
Rhegmatogenous retinal detachment	1 (0.4)	0	0
Retinal tear	0	1 (0.4)	1 (0.4)
Vitreous hemorrhage	2 (0.8)	1 (0.4)	1 (0.4)
Lens damage	0	0	1 (0.4)

ELSEVIER

Ophthalmology
Volume 116, Issue 1, January 2009, Pages 57-65.e5

Original article

Ranibizumab versus Verteporfin Photodynamic Therapy for Neovascular Age-Related Macular Degeneration: Two-Year Results of the ANCHOR Study

David M. Brown MD [1], Mark Michels MD [2], Peter K. Kaiser MD [3], Jeffrey S. Heier MD [4], Judy P. Sy PhD [5], Tsontcho Ianchulev MD, MPH [5]

Table 7. Key Adverse Event Findings: Cumulative for 2 Years of ANCHOR Study

	Verteporfin PDT (n = 143)	Ranibizumab 0.3 mg (n = 137)	Ranibizumab 0.5 mg (n = 140)
Key Serious Ocular Adverse Events—no. (%)			
Presumed endophthalmitis*	0	0	3(2.1)
Uveitis	0	0	1(0.7)*
Rhegmatogenous retinal detachment	1(0.7)†	2(1.5)	0
Retinal tear	0	0	1(0.7)
Vitreous hemorrhage	0	2(1.5)	0
Lens damage	0	0	0

Intravitreal Aflibercept (VEGF Trap-Eye) in Wet Age-related Macular Degeneration

Jeffrey S. Heier, MD,[1] David M. Brown, MD,[2] Victor Chong, MD,[3] Jean-Francois Korobelnik, MD,[4] Peter K. Kaiser, MD,[5] Quan Dong Nguyen, MD,[6] Bernd Kirchhof, MD,[7] Allen Ho, MD,[8] Yuichiro Ogura, MD,[9] George D. Yancopoulos, MD, PhD,[10] Neil Stahl, MD,[10] Robert Vitti, MD,[10] Alyson J. Berliner, MD, PhD,[10] Yuhwen Soo, PhD,[10] Majid Anderesi, MD,[11] Georg Groetzbach, MD,[11] Bernd Sommerauer, PhD,[11] Rupert Sandbrink, MD, PhD,[11] Christian Simader, MD,[13] Ursula Schmidt-Erfurth, MD,[13] for the VIEW 1 and VIEW 2 Study Groups*

Aucune donnée sur EI inflammatoire

Original article

Ranibizumab versus Bevacizumab for Neovascular Age-related Macular Degeneration: Results from the GEFAL Noninferiority Randomized Trial

The results of GEFAL study were presented at: the Association for Research and Ophthalmology meeting, May 7, 2013, Seattle, Washington, and the Société Française d'Ophtalmologie meeting, May 11, 2013, Paris, France.

Laurent Kodjikian MD, PhD [1 2 3], Eric H. Souied MD, PhD [4 5], Gérard Mimoun MD [5 6], Martine Mauget-Faÿsse MD [7], Francine Behar-Cohen MD, PhD [8 9 10 11], Evelyne Decullier PhD [2 12 13], Laure Huot PharmD, PhD [2 12 13], Gilles Aulagner PharmD, PhD [2 3 14 15], GEFAL Study Group *

Aucune donnée sur EI inflammatoire

RANIBIZUMAB

0,7 à 1,3% de patients avec uvéite

0,05% (6 cas pour 10500 injections)

Risque IO
AVANT les nouvelles molécules anti-VEGF

ORIGINAL STUDY

NONINFECTIOUS VITRITIS AFTER INTRAVITREAL INJECTION OF ANTI-VEGF AGENTS

Variations in Rates and Presentation by Medication

Williams, Patrick D. MD; Chong, Deborah MD; Fuller, Timothy MD; Callanan, David MD

Author Information

- L'incidence inflammation « pseudo-endophtalmie » était 0.08% par IVT
  - Risque ↗ BEVA 0.10% vs. RAN (0.02%) ou AFL (0.16%)

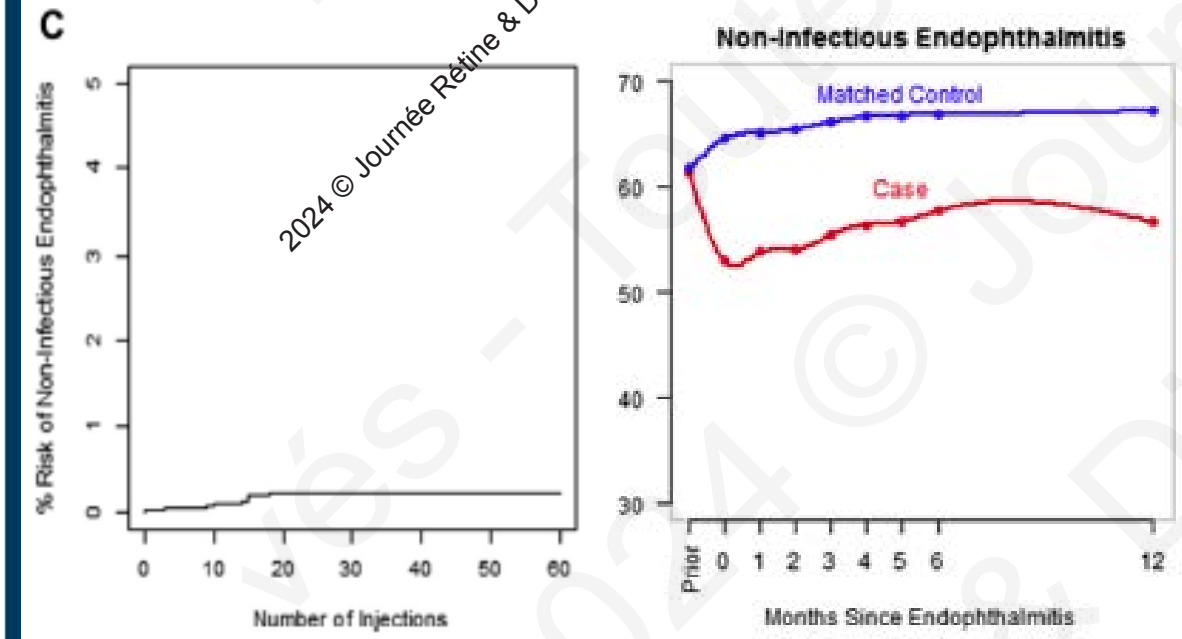
Risque inflammation
AVANT les nouvelles molécules anti-VEGF

AMERICAN ACADEMY OF OPHTHALMOLOGY™

CrossMark

Incidence and Outcomes of Infectious and Noninfectious Endophthalmitis after Intravitreal Injections for Age-Related Macular Degeneration

Vincent Daien, MD, PhD,[1,2,3] Vuong Nguyen, PhD,[1] Rohan W. Essex, MB, BS,[4] Nigel Morlet, MB, BS,[5] Daniel Barthelmes, MD, PhD,[1,6] Mark C. Gillies, MB, BS,[1] for the Fight Retinal Blindness! Study Group



incidence / IVT 0,012% (11 cas / 88150 injections)
Risque ↗ BEVA 0.08% vs RAN (0.005%) ou AFL (0%)

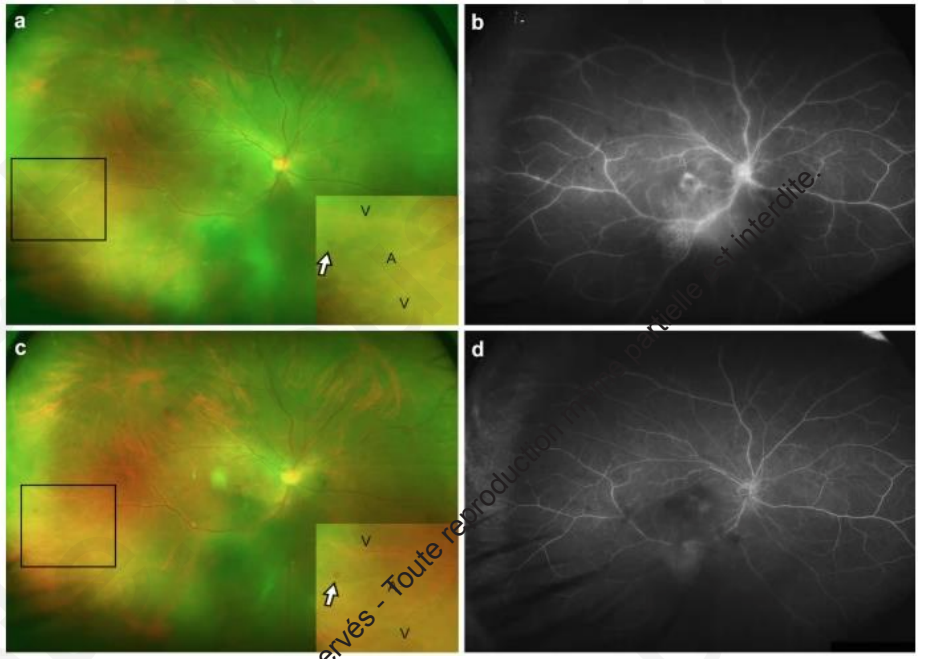
Taux cumulé par patient :
0,087% après 10 IVT
0,228% après 60 IVT

Nombre médian [Q1-Q3] IVT de 10 [3-15]

Perte d'AV en moyenne à 1 an de -6,4 lettres

Risque inflammation
AVEC les nouvelles molécules anti-VEGF

ASRS American Society of Retina Specialists



EDITORIAL · Volume 216, PA7-A8, August 2020

Download Full Issue

Is This a 737 Max Moment for Brolucizumab?

Philip J. Rosenfeld [a] · David J. Browning [b]

Affiliations & Notes · Article Info · Linked Articles (1)

Real-world Studies

Progress in Retinal and Eye Research
Volume 97, November 2023, 101219

From randomised controlled trials to real-world data: Clinical evidence to guide management of diabetic macular oedema

Pierre-Henry Gabrielle [a b], Hemal Mehta [b c], Daniel Barthelmes [b d], Vincent Daien [b e f], Vuong Nguyen [b], Mark C. Gillies [b], Catherine P. Creuzot-Garcher [a]

Clinical Trials → "Efficacy" data of an intervention

APPROVAL ↪ Regulatory Agency
FDA

"Effectiveness"
+
"Safety"
→ Evaluated from population-based observational study when "intervention" incorporated into clinical practice

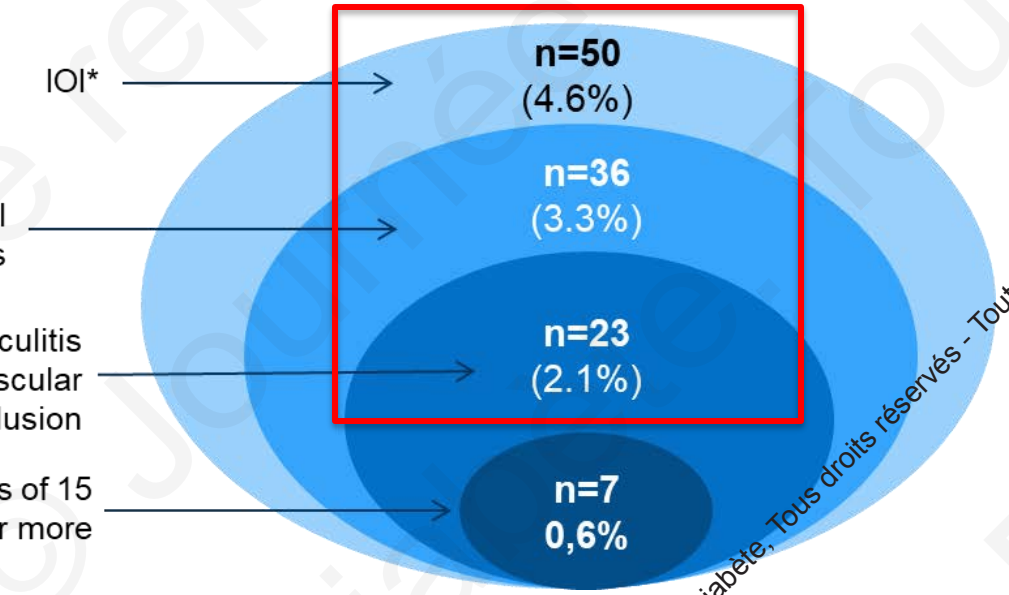
1. Sherman RE, et al. Real-World Evidence - What Is It and What Can It Tell Us? *N Engl J Med* 2016;375:2293-2297

IOI liée au brolucizumab

Post hoc Hawk & Harrier

Brolu en régime 3 Q4 + Q8 ou Q12

Population étudiée : naïve
n=1088 patients



75% IOI arrivent dans les 6 premiers mois

1. Mones J et al. Ophthalmol 2021 IOI, intraocular inflammatory; RAO, retinal artery occlusion; RO, retinal vascular occlusion; RV, retinal vasculitis. * 'La catégorie IOI' comprend les patients qui ont développé une IOI avec ou sans vascularite et avec ou sans occlusion vasculaire rétinienne. IOI, inflammation intraoculaire; SRC, Comité d'examen de la sécurité.

IO liée au brolucizumab

Inflammations intraoculaires confirmées par le Comité de Revue de Tolérance de l'étude OCTOPUS

Among the 29 patients reported by investigators with IOIs in the study eye, the SRC confirmed IOIs in 24 of these patients, while other 5 non-confirmed events were considered as non-inflammatory by the SRC (vitreous material following injection procedure)

All patients N=210	n (%)	Incident rate/total number of patients	Number of injections	Incident rate/1000 injections
IOI only	16 (7.6)	7.62	1169	13.69
IOI + Retinal vasculitis	4 (1.9)	1.90	1169	3.42
IOI + Retinal vasculitis + Retinal vascular occlusion	4 (1.9)	1.90	1169	3.42

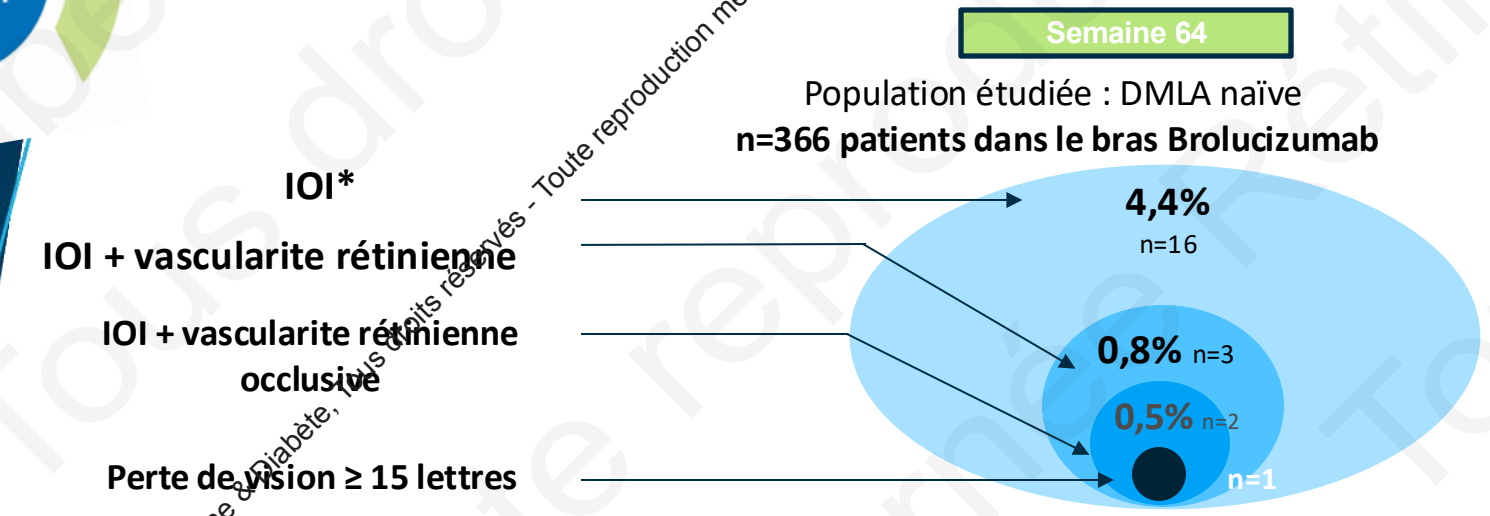
IO liée au brolucizumab

Inflammations intraoculaires confirmées par le Comité de Revue de Tolérance de l'étude SWIFT

Parmi les 42 patients rapportés par les investigateurs avec des IOI dans l'œil étudié, le SRC a confirmé des AESI chez 29 de ces patients, les 13 autres événements non confirmés ont été considérés comme non inflammatoires par le SRC (matériels vitréens après la procédure d'injection)

All patients N=295	n (%)	Incident rate/patient	Number of injections	Incident rate/1000 injections
IOI only	20 (6.8)	0.068	1654	12.50
IOI + Retinal vasculitis	6 (2.0)	0.020	1654	3.63
IOI + Retinal vasculitis + Retinal vascular occlusion	1 (0.3)	0.003	1654	0.60
IOI + Retinal vascular occlusion	2 (0.7)	0.007	1654	1.21

IO liée au brolucizumab



	Semaine 32		Semaine 64	
	Brolucizumab 6 mg (N=366), n (%)	Aflibercept 2 mg (N=368), n (%)	Brolucizumab 6 mg (N=366), n (%)	Aflibercept 2 mg (N=368), n (%)
Patients with at least one event	20 (5.5)	4 (1.1)	22 (6.0)	6 (1.6)
Patients with at least one endophthalmitis event	1 (0.3)	0	1 (0.3)	0
Patients with at least one IOI event*	14 (3.8)	3 (0.8)	16 (4.4)	5 (1.4)
Retinal occlusive vasculitis	*2 (0.5)*	*0*	2 (0.5)	0
Retinal vasculitis	*1 (0.3)*	*0*	1 (0.3)	0
Patients with at least one retinal vascular occlusion event	5 (1.4)	1 (0.3)	5 (1.4)	1 (0.3)

Après la semaine 32 :

2 nouveaux cas d'IOIs dans le bras brolucizumab (1 uvéite + 1 iritis)

2 nouveaux cas d'IOIs dans le bras aflibercept

La catégorie IOI comprend les patients qui ont développé une IOI avec ou sans vascularite et avec ou sans occlusion vasculaire rétinienne. IOI, inflammation intraoculaire.

RTH258 (Brolucizumab) - Clinical Study Report. Study no. CRTH258A2303, EudraCT no. 2019-000716-28 ; Developement phase IIIb.
29 Jan 2024 : p.2, 15, 16, 17, 18, 19, 21, 48, 49, 50, 51, 52, 58, 59, 61, 62, 63, 70, 71, 73, 74, 80, 83, 84, 89, 90, 91.

IO liée au brolucizumab

Tolérance Kite et Kestrel à 2 ans

Adverse Event	KESTREL			KITE	
	Brolucizumab 3 mg (n=190)	Brolucizumab 6 mg (n=189)	Aflibercept 2 mg (n=187)	Brolucizumab 6 mg (n=179)	Aflibercept 2 mg (n=18[illegible])
Patients with ≥1 AE, n (%)*					
Ocular (study eye)	103 (54.2)	92 (48.7)	94 (50.3)	73 (40.8)	74 (40.9)
Nonocular	146 (76.8)	146 (77.2)	143 (76.5)	136 (76.0)	141 (77.9)
Patients with ≥1 serious AE, n (%)*					
Ocular (study eye)	8 (4.2)	7 (3.7)	5 (2.7)	5 (2.8)	3 (1.7)
Nonocular	48 (25.3)	53 (28.0)	54 (28.9)	48 (26.8)	58 (32.0)
Patients with ≥15 letter loss from baseline at Week 100, n (%)†	6 (3.2)	4 (2.1)	2 (1.1)	4 (2.2)	6 (3.3)
Death, n (%)	4 (2.1)	8 (4.2)	7 (3.7)	13 (7.3)	9 (5.0)
AEs of special interest (study eye), n (%)					
Endophthalmitis	2 (1.1)	-	1 (0.5)	2 (1.1)	1 (0.6)
Intraocular inflammation[a]	10 (5.3)	8 (4.2)	2 (1.1)	4 (2.2)	3 (1.7)
- including Retinal vasculitis[a]	3 (1.6)	1 (0.5)		-	-
Retinal vascular occlusion	3+ (1.6)	3# (1.6)	1 (0.5)	1[b] (0.6)	1[b] (0.6)

Medical Dictionary for Regulatory Activities Version 24.1 (KESTREL) and 24.0 (KITE) used for the reporting of adverse events.
AE with a start date on or after the date of first study treatment administration were counted. *A patient with multiple occurrences of an AE for a preferred term or system organ class was counted only once in each specific category. [a] Percentages of patients with intraocular inflammation and percentages of patients with retinal vasculitis cannot be added up. [b]No patient with both RO and IOI in KITE
Safety Analysis Set; † Full Analysis Set-LOCF; + 2 patients experienced also IOI; # 1 patient experienced also IOI; AE, adverse event; LOCF, last observation carried forward, RO, retinal vascular occlusion; RV, retinal vasculitis

Laude et al APVRS nov 2022

IO liée au brolucizumab

Tolérance Kingfisher à 1 an

Adverse Event	Brolucizumab 6 mg (n=346)	Aflibercept 2 mg (n=171)
Patients with ≥1 AE, n (%)*		
Ocular (study eye)	105 (30.3)	59 (34.5)
Nonocular	209 (60.4)	96 (56.1)
Patients with ≥1 SAE, n (%)*		
Ocular (study eye)	3 (0.9)	0 (0.0)
Nonocular	69 (19.9)	36 (21.1)
Patients with ≥15 letter loss from baseline at Week 52, %	3/342 (0.9)	0/170 (0.0)
Death, n (%)	7 (2.0)	5 (2.9)
AESIs, study eye, n (%)		
Intraocular inflammation†	14 (4.0)	5 (2.9)
Retinal vasculitis†	3 (0.9)	1 (0.6)
Retinal vascular occlusion	1 (0.3)	1 (0.6)

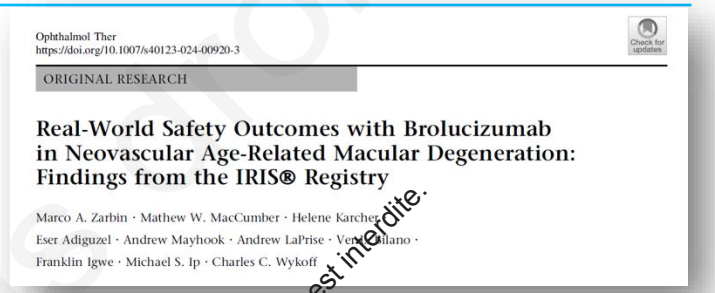
aucune occlusion n'était associée à une inflammation ou vascularite

Safety Analysis Set. Medical Dictionary for Regulatory Activities Version 24.0 used for the reporting of AEs. AE with a start date on or after the date of first study treatment administration were counted. AEs started after the subject discontinued study treatment and started alternative DME treatment in the study eye are censored. *A patient with multiple occurrences of an AE for a preferred term or system organ class was counted only once in each specific category. †A subject who experienced retinal vasculitis might have experienced other IOI AESIs also and therefore might have counted under IOI as well. AE, adverse event; AESI, adverse event of special interest; IOI, intraocular inflammation; SAE, serious adverse event

Barakat et al EURETINA sept 2022

IO liée au brolucizumab

Registre IRIS : Safety du Brolucizumab en « vraie vie » avec un suivi de 2 ans


Ophthalmol Ther
https://doi.org/10.1007/s40123-024-00920-3

ORIGINAL RESEARCH

Real-World Safety Outcomes with Brolucizumab in Neovascular Age-Related Macular Degeneration: Findings from the IRIS® Registry

Marco A. Zarbin · Mathew W. MacCumber · Helene Karcher · Eser Adiguzel · Andrew Mayhook · Andrew LaPrise · Vera Bolano · Franklin Igwe · Michael S. Ip · Charles C. Wykoff

18 312 yeux (15 998 patients) traités par brolucizumab pour une DMLA et qui ont été **suivis pendant ≤ 2 ans** après la première injection

- 614/18 312 yeux (**3,4 %**) ont subi un événement **IOI, RV et/ou RO**
  - Incidence globale **VR et/ou OR : 0,5%**

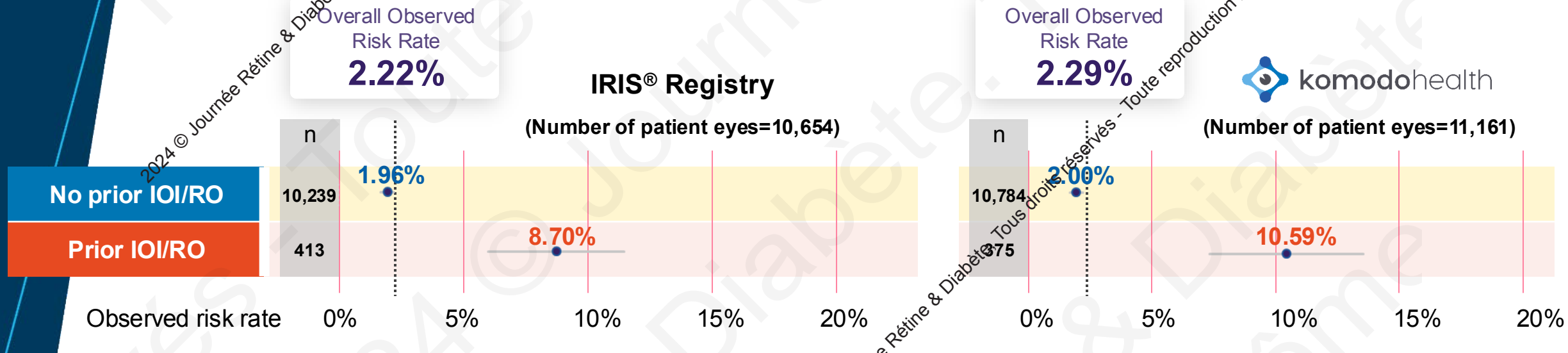
- Délai médian avant événement : **84 (42 à 167) jours (< 6 mois)**
- Nombre médian d'IVT de brolucizumab avant un événement était de **2 (1–4) (phase de bolus)**

- Médiane de BAV, post suivi de 6 mois, versus pré événement était de **0 (− 7 à + 5)**

- Facteurs de risque d'IO :
  - **Femme**
  - **Jeune**
  - **patient prétraités**
  - **patients qui ont bénéficié du brolucizumab lors de la 1e année de son lancement**

IO liée au brolucizumab

Risque x 4 à 5 d'IOI et/ou RO chez les patients ayant déjà eu un épisode IOI/RO



IOI, Intraocular Inflammation; RO, Retinal vascular occlusion inclusive of RVO and RAO; RV, Retinal Vasculitis. Based on 12-month history data; In patient eyes with up to 6 months of follow-up. Estimates for risk (95% CIs) were adjusted for age, prior anti-VEGF treatment and length of follow up. In the multivariable model, patient eyes with 'RV and/or RO' were compared to patient eyes with 'no IOI or RV or RO'.
[a]Represents IOI or Endophthalmitis or Panuveitis or RV or RO.
Khanani AM, et al. JAMA Ophthalmol. 2022; IRIS & KOMODO.

IO liée au brolucizumab

Sélection des patients (1,5,6)

- Patient sans historique d'IOI et/ou de RV
- Patient sans IOI active au moment d'injecter
- Prise en compte de l'état cognitif du patient
- Patient non monophtalme

Education du patient

Education aux symptômes (1)

Myodésopsies (>2j post-IVT)

Baisse Acuité visuelle

Douleur oculaire / oeil rouge

Sensibilité à la lumière

Engager le patient à être réactif dès les premiers signes et proposer un rendez-vous rapide si symptômes (1)

Surveillance

Examen approfondi de l'oeil avant l'injection

Outils proposés dans la littérature (1, 2,3)

- Lampe à fente dilatée,
- Fond d'oeil dilaté,
- OCT

Pendant combien de temps? (10)
80% des EI interviennent pendant la phase d'induction.

Régime de traitement

AMM[5]: Dose de charge de 3Q4 ou alternative de 2 ou 3 Q6 en fonction de l'activité de la maladie

« Le médecin peut **individualiser les intervalles de traitement selon l'activité** de la maladie »

Ne doit pas être administré plus fréquemment que tous les 2 mois après la dose de charge (4)

Holz et al. 2022 – 2. Sadda et al., ophthalmologica, 2022 3. Khoramnia et al. 2022 – 4. Khanani et al Ophthalmology 2022; MERLN 5. RCP Brolucizumab 6. Khanani AM et al. JAMA Ophthalmol. 2022;. IRIS&KOMODO 7- Bilgic A et J. Clin. Med. 2021; PROBE 8- Bilgic A, et al. J. Clin. Med. 2021; REBA. 9- Regillo et al. Talon Study 64 weeks, Angiogenesis Congress, 2023 . Gaweg et al. Brolucizumab in Neovascular Age-Related Macular Degeneration and abetic Macular Edema. Ophthalmology and Diabetology Treatment Aspects. Ophthalmol Ther. 2023 . 10 Bodaghi B., et al. Detection and management of intraocular inflammation after brolucizumab treatment for neovascular age-lated macular degeneration. Ophthalmology Retina (2023) 11. Michele Cavalleri et al. Real-Life Experience and Predictors of Visual Outcomes with Intravitreal Brolucizumab Switch for Treatment of Neovascular Age-Related Macular egeneration. Ophthalmologica 2023

IO liée au faricimab

DME and nAMD: Faricimab was well tolerated through year 2 in YOSEMITE/RHINE and TENAYA/LUCERNE

AEs Through Study End, Patients With ≥ 1 AE, n (%)[a]	Pooled YOSEMITE/RHINE			Pooled TENAYA/LUCERNE	
	Faricimab Q8W n = 630	Faricimab PTI n = 632	Aflibercept Q8W n = 625	Faricimab Up to Q16W n = 664	Aflibercept Q8W n = 662
Ocular AEs[b]	313 (49.7%)	311 (49.2%)	284 (45.4%)	358 (53.9%)	345 (52.1%)
Serious ocular AEs[b]	26 (4.1%)	34 (5.4%)	20 (3.2%)	29 (4.4%)	29 (4.4%)
Ocular AEs of special interest[c]	25 (4.0%)	33 (5.2%)	20 (3.2%)	25 (3.8%)	27 (4.1%)
Intraocular inflammation events[d]	9 (1.4%)	11 (1.7%)	7 (1.1%)	20 (3.0%)	15 (2.3%)
Uveitis	3 (0.5%)	4 (0.6%)	0	4 (0.6%)	3 (0.5%)
Iritis	1 (0.2%)	4 (0.6%)	2 (0.3%)	8 (1.2%)	3 (0.5%)
Iridocyclitis	2 (0.3%)	3 (0.5%)	1 (0.2%)	2 (0.3%)	1 (0.2%)
Vitritis	2 (0.3%)	0	2 (0.3%)	4 (0.6%)	1 (0.2%)
Post-procedural inflammation	1 (0.2%)	1 (0.2%)	2 (0.3%)	0	5 (0.8%)
Chorioretinitis	0	1 (0.2%)	0	1 (0.2%)	0
Keratic precipitates	0	1 (0.2%)	0	2 (0.3%)	0
Non-infectious endophthalmitis	0	0	0	0	1 (0.2%)
Keratouveitis	0	1 (0.2%)	0	0	0
Anterior chamber flare	0	0	0	0	1 (0.2%)
Endophthalmitis events	2 (0.3%)	4 (0.6%)	1 (0.2%)	3 (0.5%)	2 (0.3%)
Retinal vasculitis events	0	0	0	0	0
Retinal occlusive events*					
Retinal vein occlusion	1 (0.2%)	4 (0.6%)	0	0	0
Retinal artery occlusion	1 (0.2%)	2 (0.3%)	2 (0.3%)	0	0
Retinal artery embolism	0	0	1 (0.2%)	1 (0.2%)[f]	0
Arterial occlusive disease	0	0	1 (0.2%)	0	0
Serious nonocular AEs	175 (27.8%)	161 (25.5%)	173 (27.7%)	138 (20.8%)	162 (24.5%)
APTC events[e]	34 (5.4%)	30 (4.7%)	32 (5.1%)	22 (3.3%)	20 (3.0%)

IO liée au faricimab

RVO: Faricimab Was Well Tolerated, With a Safety Profile Similar to That of Aflibercept Through Week 24 in BALATON/COMINO

	BALATON (BRVO)		COMINO (H/CRVO)	
AEs Through Week 24, Patients With ≥ 1 AE, n (%)	Faricimab 6.0 mg n = 276	Aflibercept 2.0 mg n = 274	Faricimab 6.0 mg n = 365	Aflibercept 2.0 mg n = 361
Ocular AEs	45 (16.3%)	56 (20.4%)	84 (23.0%)	100 (27.7%)
Serious ocular AEs	3 (1.1%)	2 (0.7%)	9 (2.5%)	12 (3.3%)
Ocular AEs of special interest	1 (0.4%)	2 (0.7%)	8 (2.2%)	12 (3.3%)
Intraocular inflammation events	1 (0.4%)*	0	8 (2.2%)	4 (1.1%)
Vitritis	0	0	3 (0.8%)	0
Iritis	0	0	2 (0.5%)	2 (0.6%)
Uveitis	0	0	2 (0.5%)[a]	1 (0.3%)
Noninfectious endophthalmitis	0	0	0	1 (0.3%)
Iridocyclitis	0	0	1 (0.3%)	0
Endophthalmitis events	0	0	0	1 (0.3%)
Retinal vasculitis events	0	0	0	0
Retinal artery occlusion/embolism[b]	0	0	3 (0.8%)	2 (0.6%)
Serious nonocular AEs	9 (3.3%)	16 (5.8%)	22 (6.0%)	23 (6.4%)
APTC events	3 (1.1%)	4 (1.5%)	4 (1.1%)	5 (1.4%)
AEs leading to treatment discontinuation through week 24	1 (0.4%)	1 (0.4%)	3 (0.8%)	3 (0.8%)

IO liée au faricimab

Roche sponsored real-world studies

Real-World Study	FARETINA[5] a retrospective, observational, multicenter, real-world study of faricimab in patients with nAMD or DME and participating in the AAO IRIS® registry		FARWIDE[6] a retrospective, real-world study of Faricimab in patients with nAMD or DMO using medisoft EMR data from NHS sites in the UK	
Data cut-off	Feb 2022 - June 2023*		June 2022 - Feb 2024	
Eyes, n	> 70’000		18’320	
Population	Treatment naïve	Previously treated	Treatment naïve	Previously treated
Injections, n	19’274	242’229	31’457	68’111
Intraocular inflammation, n per injection	0.13%	0.11%	0.12%	0.12%
Endophthalmitis, n per injection	0.07%	0.07%	0.09%*	0.08%*

*initiating treatment

*potentially infectious endophthalmitis

[5]Ali et al., ASRS 2024; [6]Pearce et al., ASRS 2024

IO liée au faricimab

Independent real-world studies

Real-World Study	TRUCKEE[1] an independent, physician-led, multicenter, real-world study of faricimab in patients with nAMD	Wills Eye Hospital[2] an independent, retrospective, single center, real-world study of faricimab in patients with nAMD or DME	RCA[3] an independent, retrospective, multicenter, study of consecutive patients with nAMD or DME	Moorfields Eye Hospital[4] an independent, retrospective review of EMR conducted for patients with nAMD or DMO receiving faricimab
Data cut-off	Cumulative to Aug 2024	Mar 2022 - Feb 2023	Cumulative to Dec 2023	Sep 2022 - Nov 2023
Eyes, n	3’607	918	9’580	2’631
Injections, n	17’829	4’517	61’593	13’247
Intraocular inflammation, n per injection	**0.11%**	**0.2%**	**0.01%***	**0.17%**
Endophthalmitis, n per injection	0.024%	0.1%	0.048%**	excluded

*sterile endophthalmitis
**infectious endophthalmitis

[1]Graff et al., EURETINA 2024; [2]Momenaei et al., Ophth Ret 2023; [3]Yuan et al., Macula Society 2024, [4]Montesel et al., ARVO 2024

Cas inflammation post FARICIMAB à Dijon

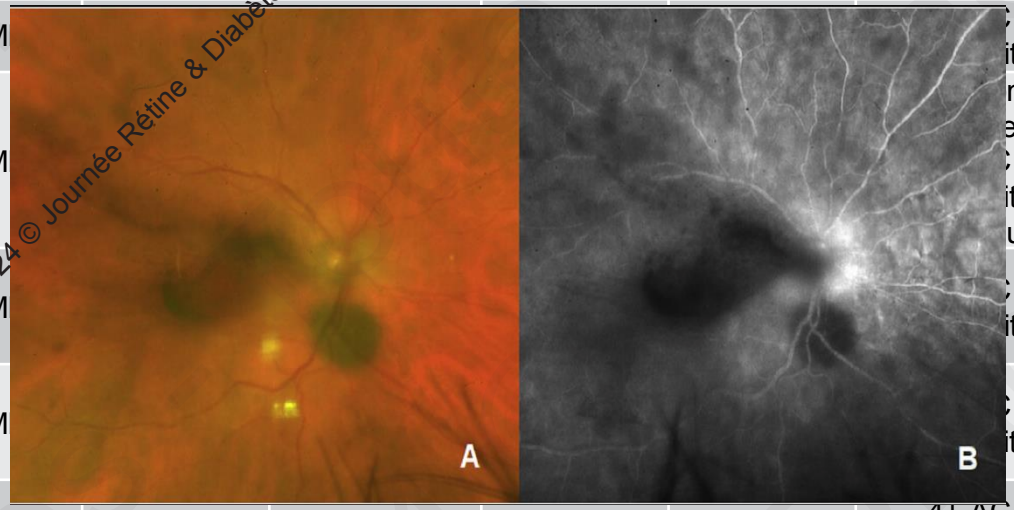
Sur 343 yeux (263 patients) traités par IVT FARICIMAB (total 971 IVTs) sur 4 mois

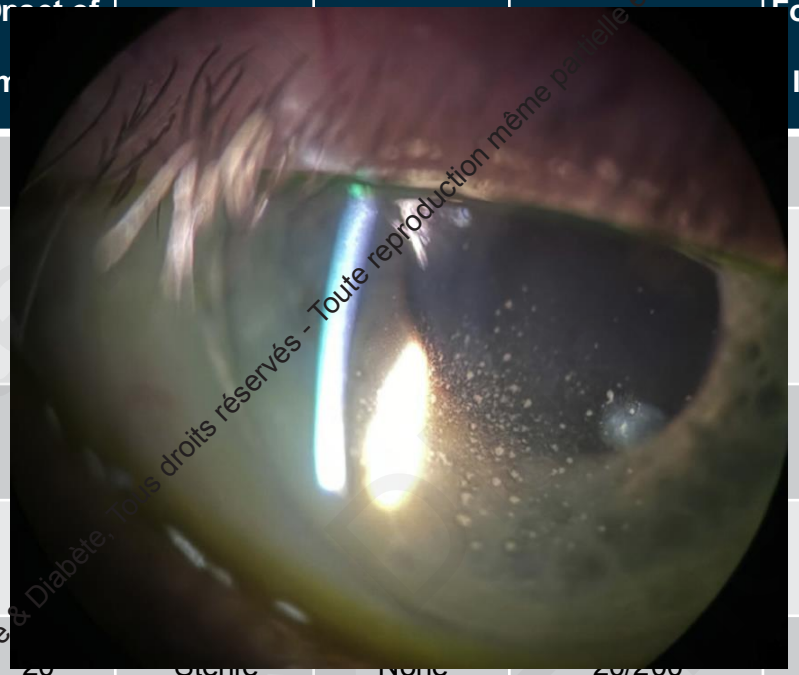
6 cas inflammations (pour 971 IVT soit 0,62%)

5 pseudo-endophtalmies et 1 UAA

Résolutif sous traitement anti-inflammatoire

Case	Faricimab indication	No. Of Faricimab IVTs	Number of days between last Faricimab IVT and IOI Onset	Baseline VA	VA at the Onset of IOI	Clinical Presentation	IOP at the Onset of (m				Duration of Follow-up Since Intraocular Inflammation (weeks)
1	nAM					C cells itritis					16
2	nAM					matous ecipitates C cells itritis ulitis					11
3	nAM					C cells itritis					2
4	nAM					C cells itritis					2
5	nAMD	5	1	20/32	20/600	4+ AC cells 2+ Vitritis	20	Sterile	None	20/200	2
6	nAMD	5	1	20/63	20/125	Granulomatous keratic precipitates 4+ AC cells	18	Not performed	None	20/63	2





Inflammations liées aux anti-VEGF (**unpublished**) Données préliminaires du registre FRB!

These are the data we currently have for AUS + EUR. The other drug incidences are from July 2022 when all the IOI fields were included

	Faricimab (N=6134)		Aflibercept (N=14106)			Ranibizumab (N=4980)			Bevacizumab (N=3991)			Brolucizumab (N=1953)		
	N	Risk (95% CI)	N	Risk (95% CI)	*P**	N	Risk (95% CI)	*P**	N	Risk (95% CI)	*P**	N	Risk (95% CI)	*P**
Intraocular inflammation	14	0.2% (0.1-0.4%)	8	0.06% (0.02-0.1%)	0.002	1	0.02% (5e-04-0.1%)	0.003	2	0.05% (0.006-0.2%)	0.04	24	1.2% (0.8-1.8%)	<0.001
Anterior uveitis	9	0.1% (0.07-0.3%)	7	0.05% (0.02-0.1%)	0.03	1	0.02% (5e-04-0.1%)	0.03	2	0.05% (0.006-0.2%)	0.04	12	0.6% (0.3-1.1%)	0.001
Chorioretinitis	0	0% (0-0.06%)	0	0% (0-0.03%)	1.00	0	0% (0-0.07%)	1.00	0	0% (0-0.09%)	1.00	0	0% (0-0.2%)	1.00
Vitritis	5	0.08% (0.03-0.2%)	1	0.007% (2e-04-0.04%)	0.01	0	0% (0-0.07%)	0.07	0	0% (0-0.09%)	0.16	15	0.8% (0.4-1.3%)	<0.001
Occlusive retinal vasculitis	1	0.02% (4e-04-0.09%)	1	0.007% (2e-04-0.04%)	0.51	0	0% (0-0.07%)	1.00	0	0% (0-0.09%)	1.00	3	0.2% (0.03-0.4%)	0.046
Non-occlusive retinal vasculitis	0	0% (0-0.06%)	0	0% (0-0.03%)	1.00	0	0% (0-0.07%)	1.00	0	0% (0-0.09%)	1.00	4	0.2% (0.06-0.5%)	0.003
Non-infectious endophthalmitis	2	0.03% (0.004-0.1%)	0	0% (0-0.03%)	0.09	0	0% (0-0.07%)	0.51	0	0% (0-0.09%)	0.52	2	0.1% (0.01-0.4%)	0.25

* Fisher's exact test was used to compare the risks of IOI between that drug and faricimab.

The unit of analysis is injections rather than eyes.

Intraocular inflammation consists anterior uveitis, chorioretinitis, vitritis, occlusive retinal vasculitis, non-occlusive retinal vasculitis and non- infectious endophthalmitis.

The period used for the analyses was after 4 July 2022, when all the components of the intraocular inflammation became available.

The first nine injections for each agent for each eye were included because we assumed the IOI occurred in the early stage after the initiation of a certain drug such as 1-9 times injections rather than ≥10 times injections.

The same sort of adverse events that occurred multiple times within 3 months were counted once.

Note that the number of intraocular inflammations does not add up to the breakdown because some eyes had multiple types of intraocular inflammation

Take Home message

- Inflammation intraoculaire peut survenir avec l'ensemble des anti-VEGF autorisés
- Les nouveaux anti-VEGF nous ont permis de mieux détecter et traiter les IO liées aux anti-VEGF
- Les inflammations oculaires semblent plus fréquentes avec les nouvelles molécules en pratique clinique courante
- Brolucizumab : 2-10% IO avec 0.2-2% RV et/ou RO en fonction de la population et type d'étude
  - PDR: ATCDT IO, patient prétraité, jeune, femme
  - 80% des IO apparaissent dans les 6 mois de l'introduction (possible après la première IVT)
  - Recommandations AMM Bolus de 3Q4 ou 3Q6 puis ≥Q8
- Faricimab : 0,1-3% IO avec 0-0,02% RV et/ou RO en fonction de la population et type d'étude
  - Médiane de 3 IVT avant l'apparition de l'inflammation
- Education du patient sur les symptômes et un examen approfondi dans les premiers 6 mois de l'introduction d'une nouvelle molécules anti-VEGF

THANK YOU FOR YOUR ATTENTION