

dexamethasone intravitreal implant for retinal vein occlusion in the USA. *Eye* 2017; **31**: 551–559.

- 2 Campochiaro PA, Brown DM, Awh CC, Lee SY, Gray S, Saroj N *et al*. Sustained benefits from ranibizumab for macular edema following central retinal vein occlusion: twelve-month outcomes of a phase III study. *Ophthalmology* 2011; **118**(10): 2041–2049.
- 3 Coscas G, Augustin A, Bandello F, de Smet MD, Lanzetta P, Staurengi G *et al*. Retreatment with Ozurdex for macular edema secondary to retinal vein occlusion. *Eur J Ophthalmol* 2014; **24**(1): 1–9.
- 4 Callanan DG, Loewenstein A, Patel SS, Massin P, Corcostegui B, Li XT *et al*. A multicenter, 12-month randomized study comparing dexamethasone intravitreal implant with ranibizumab in patients with diabetic macular edema. *Graefes Arch Clin Exp Ophthalmol* 2017; **225**(3): 463–473.
- 5 Călugăru D, Călugăru M. Ophthalmic technology assessment: therapies for macular edema associated with central retinal vein occlusion: a report by the American Academy of Ophthalmology. *Ophthalmology* 2015; **122**(11): e65–e66.

D Călugăru and M Călugăru

Department of Ophthalmology, University of Medicine Cluj-Napoca/Romania, Cluj-Napoca, Romania
E-mail: mihai.calugaru@mail.dntcj.ro

Eye (2017) **31**, 1112–1113; doi:10.1038/eye.2017.12;
published online 17 March 2017

Sir,
Response to Comment on: Treatment patterns of ranibizumab intravitreal injection and dexamethasone intravitreal implant for retinal vein occlusion in the USA

We are grateful that Dan and Mihai Călugăru¹ took interest in our article. The subject of optimal intensity of anti-VEGF treatment has been discussed previously following the publication of a similar claims data study, which described real-world treatment patterns of ranibizumab and aflibercept for macular oedema secondary to central retinal vein occlusion.^{2–4} Our study aimed to understand whether the frequency of ophthalmology visits for patients treated with ranibizumab (Lucentis) and dexamethasone implant (Ozurdex) differed in routine clinical practice in the United States for the treatment of macular oedema secondary to retinal vein occlusion (RVO).⁵ Comparing treatment frequency was a secondary objective in our study, with the resulting estimate of ranibizumab treatment frequency being consistent with that previously observed by Lotery and Regnier.²

We agree with Dan and Mihai Călugăru that the observed treatment patterns in our analysis should not be interpreted as the optimal treatment frequency. The frequency of treatment administration neither reflects the treatment frequency observed in clinical trials^{6,7} nor provides data on visual acuity outcomes attained by the treated cohort. In our discussion, we outline the limitation that visual acuity data

were not available in the claims database at our disposal for the conduct of this study.⁵

The Callanan *et al.* study aimed to demonstrate the non-inferiority of dexamethasone implant compared to ranibizumab with respect to mean average change from baseline best-corrected visual acuity (BCVA) over 12 months in patients with diabetic macular oedema. The primary outcome of non-inferiority between treatments was met; however, statistically significant and clinically meaningful differences were observed in mean change from baseline in BCVA favouring ranibizumab. Furthermore, a saw-tooth pattern in central retinal thickness (CRT), indicative of frequent fluctuation of CRT, was observed in the dexamethasone arm. This is in contrast to the sustained improvements in CRT for ranibizumab-treated eyes during the study period.⁸ Superiority of dexamethasone implant *vs* ranibizumab in anatomical outcomes was not demonstrated in the Callanan study. Moreover, the authors did not find the claim of superior anatomical outcomes associated with dexamethasone implant adequately supported by randomised clinical trial evidence.¹

Studies linking treatment patterns to real-world clinical outcomes in RVO will be an important part of understanding outcomes attained by patients in routine clinical practice.

Conflict of interest

SN-B and SB are consultants for Allergan, Bayer and Novartis. SR is an employee of Novartis Pharma AG, Basel, Switzerland. A Skelly is an employee of Novartis Pharma AG, Basel, Switzerland. NY was an employee of IMS Health, London, UK, at the time of the original study, funded by Novartis to perform the statistical analyses for the study, but was not involved in the collection of the dataset or in gaining access to it for the purposes of the study. A Sodi is a member of the Novartis RVO advisory board.

References

- 1 Călugăru D, Călugăru M. Treatment patterns of ranibizumab intravitreal injection and dexamethasone intravitreal implant for retinal vein occlusion in the USA. *Eye (Lond)* 2017; **31**: 1112–1113.
- 2 Lotery AJ, Regnier S. Patterns of ranibizumab and aflibercept treatment of central retinal vein occlusion in routine clinical practice in the USA. *Eye (Lond)* 2015; **29**: 380–387.
- 3 Călugăru D, Călugăru M. Patterns of ranibizumab and aflibercept treatment of central retinal vein occlusion in routine clinical practice in the USA. *Eye (Lond)* 2015; **29**: 1113.
- 4 Lotery A, Regnier S. Response to 'Patterns of ranibizumab and aflibercept treatment of central retinal vein occlusion in routine clinical practice in the USA'. *Eye (Lond)* 2015; **29**(8): 1113–1114.
- 5 Nghiem-Buffet S, Baillif S, Regnier S, Skelly A, Yu N, Sodi A. Treatment patterns of ranibizumab intravitreal injection and dexamethasone intravitreal implant for retinal vein occlusion in the USA. *Eye (Lond)* 2017; **31**: 551–559.
- 6 Brown DM, Campochiaro PA, Singh RP, Li Z, Gray S, Saroj N *et al*. Ranibizumab for macular edema following

central retinal vein occlusion. six-month primary end point results of a phase III study. *Ophthalmology* 2010; 117: 1124–1133.

- 7 Campochiaro PA, Heier JS, Feiner L, Gray S, Saroj N *et al.* for the BRAVO Investigators Ranibizumab for macular edema following branch retinal vein occlusion. six-month primary end point results of a phase III study. *Ophthalmology* 2010; 117: 1102–1112.
- 8 Callanan DG, Loewenstein A, Patel SS, Massin P, Corcostegui B, Li XT *et al.* A multicenter, 12-month randomized study comparing dexamethasone intravitreal implant with ranibizumab in patients with diabetic macular edema. *Graefes Arch Clin Exp Ophthalmol* 2016; e-pub ahead of print 8 September 2016.

S Nghiem-Buffet^{1,2}, S Baillif³, S Regnier⁴, A Skelly⁵, N Yu⁶ and A Sodi⁷

¹Centre Ophtalmologique d'Imagerie et de Laser, Paris, France

²Department of Ophthalmology, Hôpital Avicenne, Assistance Publique, Hôpitaux de Paris and Paris 13 University, Bobigny, France

³Department of Ophthalmology, Pasteur II University Hospital, Nice, France

⁴Novartis Pharma AG, Basel, Switzerland

⁵Novartis Ireland Limited, Dublin, Ireland

⁶Real-World Evidence Solutions, IMS Health, London, UK

⁷Department of Ophthalmology, Careggi University Hospital, Florence, Italy

E-mail: buffet.nghiem@free.fr

Eye (2017) 31, 1113–1114; doi:10.1038/eye.2017.15; published online 24 February 2017

Sir, Regarding 'Advances of optical coherence tomography in myopia and pathologic myopia'

We read with interest the article 'Advances of optical coherence tomography in myopia and pathologic myopia'.¹ In this article, the authors cite the original definition of dome-shaped macula (DSM) by Gaucher *et al*² as 'an inward bulge of the macula within the concavity of a posterior staphyloma in highly myopic eyes,' and go on to expound the 'many uncertainties' regarding DSM. Specifically, the authors outline several theories for the development of DSM: 'resistance to deformation of scleral staphyloma, scleral infolding through the collapse of the posterior portion of the eye wall, and tangential vitreoretinal traction.'¹ We would like to present a novel mechanical explanation for the development and pathophysiology of DSM based on the fundamental physical principles of Pascal's principle and Laplace's law.

Pascal's principle³ tells us that the internal pressure inside of a closed vessel, such as the eye as a whole (or a blood vessel or a tube containing fluid), is the same throughout, despite variations in radius or diameter of the vessel. Laplace's law⁴ goes on to define the relationship between the radius of that vessel and wall tension, given the constant internal pressure (Figure 1). In an enclosed vessel such as a theoretical eye with uniform elasticity and

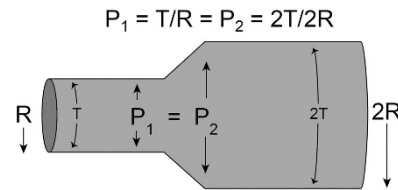


Figure 1 Laplace's Law.

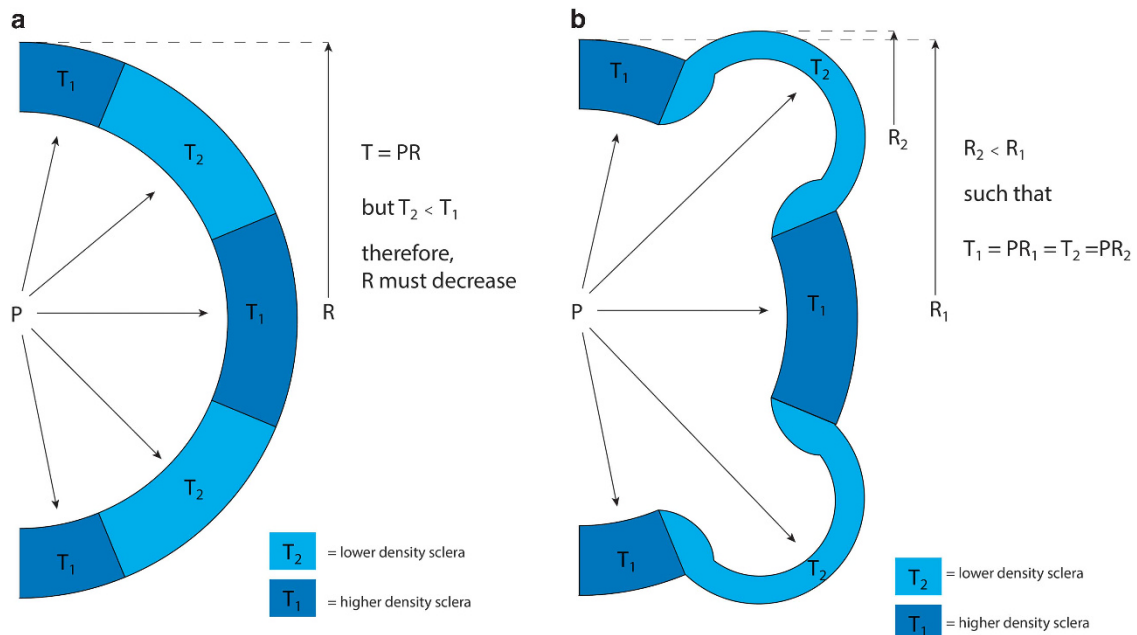


Figure 2 Pascal's Principle and Laplace's Law in Dome-Shaped Macula (DSM).