Eye (2016) 30, 1023–1028

www.nature.com/eye

Sir,
Comments on 'Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants'

We read with interest the article titled 'Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants' by Yang *et al.*[1] They present a *post hoc* analysis of the FAME study[2] and compare visual outcomes in patients undergoing cataract surgery after low-dose FAc implant with those who were pseudophakic at baseline. They conclude the former group to have possibly better long-term results.

In the cataract surgery after implant (CAI) group, the favorable change in visual acuity may have been partly contributed by removal of lenticular aberrations[3] expected in diabetes patients having early lens opacities or even lenticular swelling. Hence, crediting FAc for better visual results in the CAI group may be erroneous. Single intravitreal steroid injections have been reported to cause subcapsular cataract and multiple injections may affect all the lens layers.[4] Given the continuous low intraocular concentration of steroid with FAc implant, it would be interesting to evaluate the type of cataract seen in the CAI group.

The other adverse effect of FAc noted in the FAME study was ocular hypertension, with nearly 4% of subjects injected with low-dose FAc needing incision glaucoma surgery.[2] As lens extraction is known to decrease intraocular pressure,[5] we suggest analyzing change in intraocular pressure in patients in the CAI group after cataract surgery. It is possible that ocular hypertension may have resolved altogether in some patients, especially in the presence of anterior synechiae.

As the diabetic macular edema and its treatment are of utmost importance, we wish the authors would share their opinion on these issues.

Conflict of interest

The authors declare no conflict of interest.

References

1 Yang Y, Bailey C, Holz FG, Eter N, Weber M, Baker C *et al.* Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants. *Eye (Lond)* 2015; **29**: 1173–1180.

2 Campochiaro PA, Brown DM, Pearson A, Ciulla T, Boyer D, Holz FG *et al.* Long-term benefit of sustained-delivery fluocinolone acetonide vitreous inserts for diabetic macular edema. *Ophthalmology* 2011; **118**: 626–635.

3 Sachdev N, Ormonde SE, Sherwin T, McGhee CN. Higher-order aberrations of lenticular opacities. *J Cataract Refract Surg* 2004; **30**: 1642–1648.

4 Sarao V, Veritti D, Boscia F, Lanzetta P. Intravitreal steroids for the treatment of retinal diseases. *ScientificWorldJournal* 2014; **2014**: 989501.

5 Dada T, Rathi A, Angmo D, Agarwal T, Vanathi M, Khokhar SK *et al.* Clinical outcomes of clear lens extraction in eyes with primary angle closure. *J Cataract Refract Surg* 2015; **41**: 1470–1477.

B Takkar and S Azad

Dr Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi, India
E-mail: shoryaazad@hotmail.com

Eye (2016) **30,** 1023; doi:10.1038/eye.2016.27; published online 11 March 2016

Sir,
Reply to 'Comments on Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants'

We thank Takkar and Azad[1] for their astute observations on our recent paper[2] which focused on the outcomes of phakic patients who developed cataract after receiving fluocinolone implant and underwent cataract surgery in the FAME trial. It is quite correct of them to comment that the visual improvement seen in this group of patients could represent an over-estimation or bias if these patients had significant cataract at baseline before receiving implant. However, this is unlikely to be the case as any cataract which either prevented assessment of the fundus or which had a significant impact on visual acuity was an exclusion criterion.[3] In addition, the baseline acuities and central retinal thickness of these patients were very similar to those who were pseudophakic at baseline as shown in Table 1 (baseline characteristics) in our paper. Moreover, it would have been unlikely that small lenticular aberrations would have affected the baseline visual acuity measurements of this group of patients due to the use of high-contrast ETDRS charts and protocol refraction techniques for the measurement of visual acuities in the FAME study. The important message from our study was that patients who were phakic before receiving fluocinolone implant but developed cataract after fluocinolone implant were able to recover visual acuity well after subsequent cataract surgery. We felt it was important to highlight this finding following analysis of the long-term follow-up data on this subgroup of patients following cataract surgery, as the use of fluocinolone implant for diabetic macular oedema in UK is currently restricted by NICE guidance to only those patients who are pseudophakic. Although these guidelines have enabled patients with eyes that are pseudophakic and with persistent diabetic macular oedema following anti-vascular endothelial growth factor (VEGF) therapy to benefit from fluocinolone implant,[4] there is still an unmet need for those with diabetic macular oedema which is unresponsive to laser or anti-VEGF therapy in phakic eyes. We also agree that it would be interesting to investigate the effects of cataract surgery on steroid-induced ocular hypertension or glaucoma, but this was unrelated to the tight remit and scope of our study question and objective, and therefore, we did not include this analysis in our design.

Conflict of interest

YY: honoraria, advisory board—Alimera Sciences, Allergan, Alcon, Bayer, Novartis, Thrombogenics;

consultancy—Alimera Sciences, Allergan. CB: honoraria—Novartis; commercial funding for clinical trial recruitment via Bristol Eye Hospital—Alimera Sciences; research funding for clinical trials work via Bristol Eye Hospital—Bayer. FH: research funding, consultancy, grants, honoraria—Alimera Sciences, Allergan, Novartis. NE: research funding, speakers bureau, honoraria, advisory board—Novartis, Bayer, Allergan; speakers bureau, honoraria—Heidelberg Engineering; advisory board—Bausch and Lomb; research funding, advisory board—Alimera Sciences. MW: honoraria, advisory board—Alimera Sciences. SK: consultancy, honoraria—Alimera Sciences, Allergan, Genentech/Roche, Regeneron, speakers bureau—Allergan, Genentech/Roche, Regeneron. PD: consultancy, honoraria—Alimera Sciences, Allergan, Alcon. AL: research funding, honoraria, advisory committee—Alimera Sciences. JMRM, UM: nothing to disclose.

References

1 Takkar B, Azad S. Comments on 'Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants'. *Eye (Lond)* 2016; **30**: 1023.
2 Yang Y, Bailey C, Holz FG, Eter N, Weber M, Lotery A *et al.* Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants. *Eye (Lond)* 2015; **29**: 1173–1180.
3 Campochiaro PA, Brown DM, Pearson A, Ciulla T, Boyer D, Holz FG *et al.* Long-term benefit of sustained-delivery fluocinolone acetonide vitreous inserts for diabetic macular edema. *Ophthalmology* 2011; **118**(4): 626–635.e2.
4 Elaraoud I, Andreatta W, Kidess A, Bhatnagar A, Tsaloumas M, Quhill F *et al.* Use of fluocinolone acetonide for patients with diabetic macular oedema: patient selection criteria and early outcomes in real world setting. *BMC Ophthalmol* 2016; **16**(1): 3.

Y Yang[1], C Bailey[2], FG Holz[3], N Eter[4], M Weber[5], C Baker[6], S Kiss[7], U Menchini[8], JM Ruiz Moreno[9], P Dugel[10] and A Lotery[11] on behalf of the FAME study group

[1]Royal Wolverhampton, Hospitals NHS Trust, New Cross, Wolverhampton, UK
[2]University Hospitals Bristol, NHS Foundation Trust, Bristol, UK
[3]University of Bonn, Bonn, Germany
[4]University of Muenster Medical Center, Muenster, Germany
[5]University Hospital of Nantes, Nantes, France
[6]Paducah Retinal Center, Paducah, KY, USA
[7]Weill Cornell Medical College, New York, NY, USA
[8]Università degli Studi di Firenze, Firenze, Italy
[9]University Castilla La Mancha, Albacete, Spain
[10]Retinal Consultants of Arizona, Phoenix, AZ, USA
[11]University of Southampton, Southampton, UK
E-mail: yit.yang@nhs.net

Eye (2016) **30,** 1023–1024; doi:10.1038/eye.2016.33; published online 11 March 2016

Sir,
Treatment trials for diabetic macular oedema

In a recent review in *Eye*, Amoaku *et al*[1] identify the need for a therapy for centre-involved diabetic macular oedema (DMO) that (i) dries the retina and improves visual acuity for a significant period, (ii) reduces adverse events, treatment burden, and costs, and (iii) is well-tolerated by patients.[1] They then make the case for an intravitreal injection regime that includes both steroids and antagonists against vascular endothelial growth factor (VEGF). The rationale was based on myriad putative mechanisms of drug action together with the results of randomised controlled trials of monotherapies. Combining a steroid with an anti-VEGF agent was said to hold promise of improved anatomical and functional outcomes together with a reduction in the (otherwise monthly) regularity of injections. This is despite the fact that previous clinical trials have shown no such adjunctive benefit.[2–5]

In the experience of many vitreoretinal surgeons, a permanent cure for DMO can often be achieved by 'one-off' vitrectomy and removal of the internal limiting membrane (ILM). A neuroprotective and sustentacular role for reparative intraretinal gliosis has been invoked. Recently, the superiority of ILM peeling over other therapies for DMO has been suggested by a non-randomised study.[6] If future trials of intravitreal therapies for DMO are contemplated, one arm of the study should comprise vitrectomy and ILM peeling.

Conflict of interest

The author declares no conflict of interest.

References

1 Amoaku WM, Saker S, Stewart EA. A review of therapies for diabetic macular oedema and rationale for combination therapy. *Eye (Lond)* 2015; **29**: 1115–1130.
2 Ahmadieh H, Ramezani A, Shoeibi N, Bijanzadeh B, Tabatabaei A, Azarmina M *et al.* Intravitreal bevacizumab with or without triamcinolone for refractory diabetic macular edema; a placebo-controlled, randomized clinical trial. *Graefes Arch Clin Exp Ophthalmol* 2008; **246**: 483–489.
3 Soheilian M, Ramezani A, Obudi A, Bijanzadeh B, Salehipour M, Yaseri M *et al.* Randomized trial of intravitreal bevacizumab alone or combined with triamcinolone versus macular photocoagulation in diabetic macular edema. *Ophthalmology* 2009; **116**: 1142–1150.
4 Marey HM, Ellakwa AF. Intravitreal bevacizumab alone or combined with triamcinolone acetonide as the primary treatment for diabetic macular edema. *Clin Ophthalmol* 2011; **5**: 1011–1016.
5 Lim JW, Lee HK, Shin MC. Comparison of intravitreal bevacizumab alone or combined with triamcinolone versus triamcinolone in diabetic macular edema: a randomized clinical trial. *Ophthalmologica* 2012; **227**: 100–106.
6 Adelman R, Parnes A, Michalewska Z, Parolini B, Boscher C, Ducournau D. Strategy for the management of diabetic macular edema: the European vitreo-retinal society macular edema study. *Biomed Res Int* 2015; **2015**: 352487.