A cost analysis comparing continued 3-year aflibercept monotherapy versus a switch from aflibercept to the fluocinolone acetonide intravitreal implant in phakic patients with chronic diabetic macular edema

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ABSTRACT
Objectives: To compare the 3-year cost in the NHS in England of continued aflibercept injections with that of switching to a single fluocinolone acetonide (FAc) intravitreal implant in phakic patients with chronic diabetic macular edema (DME); that is, DME that persists or recurs despite treatment.
Methods: A cost analysis model was developed. This accounts for the overall direct cost of treatment in phakic eyes, including the costs of the drugs, administration, monitoring, additional interventions required, and adverse event management.
Results: This model shows cost savings for patients with a phakic lens when they are switched to FAc following initial aflibercept monotherapy. Using NHS list prices, the total treatment cost over a 3-year period per phakic eye is £15,413.23 with continued aflibercept monotherapy and £14,485.06 with a switch to FAc – resulting in a cost saving with FAc of £928.17 per eye over a 3-year period.
Conclusions: This cost analysis showed that switching patients with an initial suboptimal response from aflibercept to FAc was associated with a cost advantage compared with continued aflibercept injections. With increasing demand for intravitreal therapies, the true benefit of treatment with FAc may be its potential as a suitable and effective option to increase clinic capacity.

1. Introduction
Diabetic macular edema (DME) is a complication of diabetic retinopathy [1]. Landmark multicenter randomized controlled trials, such as the Diabetes Control and Complications Trial and United Kingdom Prospective Diabetes Study, have clearly established the link between the severity of retinopathy and risk factors such as duration and severity of diabetes mellitus, systemic hypertension, dyslipidaemia and smoking. From 1980 to 2014, a fourfold increase in the prevalence of diabetes mellitus has been observed worldwide, indicating the need for a global strategy to combat this disease [2]. In 2015, the prevalence of diabetes mellitus in the adult population of the UK was estimated at around 9% [3]. Diabetic eye disease is no longer the main cause of registrable blindness in the UK, but it is still the second most important cause after inheritable eye diseases [4].

Prevalence figures calculated by the National Ophthalmology Database in the UK suggest that around 10% of diabetic patients attending the hospital eye service with diabetic retinopathy have center-involving DME [4], whereas a literature review has reported a prevalence ranging from 6% to 14% [5]. Nevertheless, DME is a major public health problem and has a huge impact on the patient and healthcare provision.

The pathophysiology of DME involves the breakdown of the blood–retina barrier. This causes extravasation of fluid from the blood vessels, leading to swelling and thickening of the macula. If the accumulation of fluid involves the fovea, this can lead to visual impairment. In patients with DME, tissue damage occurs as a result of inflammation and the production of various cytokines and mediators such as vascular endothelial growth factor (VEGF), which is the target for current first-line therapy with anti-VEGF drugs [1].

Anti-VEGF drugs and steroid implants have superseded thermal laser treatment as the mainstay of treatment for DME over the past decade due to the ability of these agents to stabilize and even achieve a subjective improvement in vision [6,7]. Recent studies, however, have indicated poor visual outcomes in one-third of patients after 2 years of continued anti-VEGF treatment, which may be due to a combination of factors, including a suboptimal response to the drug administered (i.e., visual and anatomic parameters indicating that a patient is not benefiting from continued treatment), suboptimal drug delivery (i.e., inadequate delivery of the drug to the eye), and poor compliance [8–12].

The fluocinolone acetonide (FAc) intravitreal implant is a non-biodegradable, sustained-release drug delivery system of 190 μg FAc, releasing a dose of 0.2 μg per day [13]. It has a marketing license in the EU for the treatment of vision impairment associated with chronic DME considered insufficiently responsive to available therapies (i.e., DME that persists or recurs despite treatment) [13]. The FAc intravitreal implant contains a corticosteroid that has both anti-VEGF and anti-inflammatory properties [6]. Pooled data from the two pivotal FAME trials in patients (who had only received prior laser therapy) with DME previously...
indicated that the FAc intravitreal implant was more effective than sham injection when evaluating the visual outcomes (best-corrected visual acuity and central retinal thickness) [14]. This therapeutic effect was maintained at 36 months [14]. In addition, results showed that visual outcomes of phakic eyes treated with the 0.2 µg/day FAc implant were no worse than the outcomes seen in patients with pseudophakic eyes once cataracts had been removed by surgery, and similar reductions in central foveal thickness were observed in both groups [15]. The results from the FAME studies are supported by real-world evidence [16–18]: the ongoing 5-year ILUVIEN Registry Safety Study demonstrated sustained stability or improvement in visual acuity and only a small increase in intraocular pressure (IOP) [17]; furthermore, a UK audit of patient records demonstrated that mean changes in visual acuity from baseline to 2 years in patients with persistent or recurrent DME despite prior treatment were numerically similar to those in the FAME studies [18].

Importantly, however, the National Institute for Health and Care Excellence (NICE) has restricted use of the FAc intravitreal implant to patients with DME in pseudophakic eyes and does not recommend its use in phakic eyes, where it considered that cost-effectiveness has not been demonstrated [19]. This means that there is currently no effective treatment for patients with phakic eyes when a suboptimal response has been detected. As a result, effective treatment options are severely limited for phakic patients and clinicians are restricted to continued administration of therapies that display minimal improvement in visual acuity with the distressing prospect of potential loss of eyesight for the patient.

We performed a 3-year cost analysis to evaluate the potential budgetary and healthcare resource impact of treating patients with DME and a phakic lens. The analysis was designed to model two treatment pathways: (1) a current pathway of continued monotherapy with aflibercept injections despite a suboptimal response being detected after an initial loading dose (i.e., five injections, as per the summary of product characteristics) and (2) a revised pathway of switching treatment to a single FAc implant following a suboptimal response to the initial loading dose of aflibercept (this is consistent with the licensed indication for the FAc implant, although not in line with NICE guidance).

2. Methods

This is a hypothetical analysis, which assesses the cost of treating people with DME with a phakic lens (central foveal thickness > 400 µm) over a 3-year period (corresponding to the lifespan of the FAc intravitreal implant). A budget impact model (BIM) was developed to simulate the treatment costs of two scenarios (continued aflibercept or switching to the FAc after a suboptimal response to an initial loading dose of aflibercept (i.e., five injections, as per summary of product characteristics) in patients with persistent or recurrent DME and a phakic lens. Unit costs applied to healthcare resources are listed in Table 1. The costs of outpatient attendances and procedures and inpatient or day case admissions were derived using the costs detailed in the NHS National Tariff for England, UK [20].

2.1. Model structure

In scenario 1, after an initial suboptimal response to the injection of aflibercept, treatment with aflibercept continues through to year 3. This scenario is intended to represent the cost of treating a patient who receives continued aflibercept injections even though a suboptimal response could have been detected after the initial loading dose. In scenario 2 (revised pathway), treatment with aflibercept is discontinued after a suboptimal response to the initial loading dose of five injections and patients are switched to a single injection of the FAc intravitreal implant – this is consistent with the licensed indication of the FAc implant. The model structure is shown in Figure 1.

2.1.1. Scenario 1 (current pathway): continued treatment with aflibercept

In scenario 1, the model assumed that, after the initial loading dose of aflibercept (five injections), patients received an additional nine injections and follow-up visits; that is, a total of 14 aflibercept injections and 14 follow-up visits over the 3-year period. This assumption was based on the injection numbers published in the analysis by Quhill and Beiderbeck [21], which reported a median of 14 anti-VEGF (ranibizumab) injections over a 3-year period (a median of seven, four, and three injections in years 1, 2, and 3, respectively). These numbers are also consistent with those reported for aflibercept in randomized controlled trials [22]. In routine clinical practice, the number of anti-VEGF injections is likely to be lower than the licensed posology, as shown in the POLARIS study [7], where the mean number of injections in year 1 was 4.9; however, outcomes in that study were suboptimal in comparison with other randomised controlled trials. Injection numbers were modeled to decrease [21] in years 2 and 3 to account for treat-and-extend dosing regimens [23].

The total cost of aflibercept treatment included in the analysis for the 3-year period comprised: the cost of acquisition and administration of aflibercept injections, the cost of 14 follow-up appointments with optical coherence tomography (OCT) retinal imaging to monitor patients, and the cost of managing any adverse events they may develop. Based on trial data, it was assumed that, in any year, up to 7.1% of patients would have an increase in IOP ≥ 25 mmHg requiring treatment with eye drops and 0% of patients would require surgical treatment for increased IOP. It was also assumed that less than 1% would develop endophthalmitis or retinal detachment, and 6.6% would require cataract surgery in years 1, 2, and 3 [24].

2.1.2. Scenario 2 (revised pathway): switch from aflibercept to the FAc intravitreal implant

In scenario 2, the model assumed that, after the initial loading dose of aflibercept (five injections), patients would be switched to a single injection of the FAc intravitreal implant. The model assumed that the cost of a single FAc implant treatment is the sum of the cost of purchasing and administering one FAc implant and the cost of any additional aflibercept injections required. It was assumed (as this may vary in real-life practice) that 25% of eyes would require one top-up
# Table 1. Breakdown of cost calculations included in the model.

| Cost over 3 years | Item | Unit cost (£) | Aflibercept treatment | Fac treatment | | | | Year 1 | Year 2 | Year 3 | Total | Year 1 | Year 2 | Year 3 | Total |
|-------------------|------|---------------|------------------------|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Treatment over 3 years | Aflibercept injection | 816.00a | 14 injections | 5 injections | | | | | | | | | | | | | | | |
| FAc | 5,500b | – | 1 implant | – | – | – | – | | | | | | | | | | | | | |
| Administration cost per injection | | 107.00c | 14 injections | 6 injections | | | | | | | | | | | | | | | | |
| Top-up aflibercept injection: appointment (£68.00d) + OCT (£92.00e) + aflibercept (£816.000) | 1,083.00 | | | | | | | | | | | | | | | | | |
| Total treatment cost | | | | | | | | | | | | | | | | | | |
| Monitoring over 3 years | Ophthalmology outpatient follow-up appointment: appointment (£68.00d) + OCT (£93.000) | 161.00 | 14 visits | 18 visits | | | | | | | | | | | | | | | | |
| AE management over 3 years | Drug treatment of raised IOP (≥25 mmHg) (£17.75f) + 4 follow-up visits (£68.000) | 289.75 | 7.10% in Years 1, 2, and 3 | 0% | | | | | | | | | | | | | | | | |
| IOP lowering surgery (£1,208.00g) + 4 follow-up visits (£68.000) | 1,480.00 | | | | | | | | | | | | | | | | | |
| Cataract extraction (£667.00h) + 2 outpatient visits (£667.00 × 2) | 803.00 | 6.60% in Years 1, 2, and 3 | 7.66% in year 1, 29.20% in year 2, 9.60% in year 3 | 0% | | | | | | | | | | | | | | | | |
| Treatment of endophthalmitis (£1,608.00i) + 7 outpatient visits (£68.00 × 7) | 1,796.00 | 0% in year 1 and 0.4% in years 2 and 3 | 0.11% have treatment-related endophthalmitis per year | 0% | | | | | | | | | | | | | | | | |
| Treatment of retinal detachment (£1,608.00i) + 4 outpatient visits (£68.00 × 4) | 1,592.00 | 0.27% have retinal detachment per year | 0.11% have retinal detachment per year | 0% | | | | | | | | | | | | | | | | |
| Total AE management cost | | | | | | | | | | | | | | | | | | |
| Total: overall | | | | | | | | | | | | | | | | | | |

AE = adverse event; FAc = fluocinolone acetonide intravitreal implant; IOP = intraocular pressure; OCT = optical coherence tomography.

Notes:

1. https://bnf.nice.org.uk/medicinal-forms/aflibercept.html (accessed May 2018) [27].
2. https://bnf.nice.org.uk/medicinal-forms/fluocinolone-acetonide.html (accessed May 2018) [27].
3. NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: BZ86B [28].
4. NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: WF02A Follow-up attendance – multi professional [28].
5. NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: BZ81A [28].
6. Assumption based on audit of fluocinolone intravitreal implant patients in the analysis conducted by Quhill et al, 2017 [23].
7. https://bnf.nice.org.uk/medicinal-forms/latanoprost.html (accessed May 2018) [27].
8. Aflibercept summary of product characteristics 2016 [21]; Korobelnik et al. Ophthalmology 2014 [22].
9. FAME trials [14–16]; NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: BZ81C [28].
10. NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: BZ81A [28].
11. NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: BZ81C [28].
12. NHS England 2017/18 and 2018/19 National Tariff: currencies and prices: BZ81A [28].
injection each year; this assumption was based on an audit of the patients included in the analysis by Quhill and Beiderbeck [21]. The costs of monitoring the patient include the cost of 18 follow-up appointments with OCT retinal imaging and that of managing adverse events. Based on Phase III clinical trial data, it was assumed that 7.66%, 29.20%, and 9.60% of phakic eyes would require cataract surgery in years 1, 2, and 3, respectively [14, 15, 25]. These numbers are annualized incidence rates, calculated as the number of cataract surgeries divided by the number of treated phakic eyes at baseline, divided by the number of years. In addition, it was assumed that 17.7%, 8.1%, and 5.3% of patients in years 1, 2, and 3, respectively, would have an increase in IOP ≥ 25 mmHg requiring treatment with eye drops, less than 3% would require surgery to reduce raised IOP, and less than 1% would develop endophthalmitis or retinal detachment in each of the three years.

2.1.3. Cost assumptions

The total costs included in the analysis comprised the costs of treatment, monitoring, and adverse event management (Table 1). Treatment costs included those for drug acquisition and administration, and follow-up for any additional aflibercept injections needed by FAc-treated patients. The cost of laser therapy was not included in either group, based on the assumption that the use of FAc better reflects deferred laser both in the pivotal FAME studies [14] and real-world evidence where anti-VEGF is predominantly used as a supplemental therapy and macular laser is employed in less than 7% of cases [16]. Monitoring costs covered patients’ follow-up appointments and OCT retinal imaging. Costs for adverse event management included the costs of drug and/or surgical treatment of the adverse event and any additional appointments needed. The cost included in the analysis for managing an identified adverse event was determined by the frequency of the event; for example, if 0.11% of patients required treatment for endophthalmitis in each of the three years and the annual cost of endophthalmitis treatment was £1,796.00, the cost per eye included in the analysis was £5.93 (i.e., 0.11% of £1,796 multiplied by three) (Table 1).

The analysis was developed as part of a BIM and costs were, therefore, not discounted. All drug costs were based on list prices and only direct costs usually covered by the NHS in England were included. Indirect costs, such as those associated with patients and carers having to travel and take time off work to attend appointments, were not included; thus, their effect on the overall economic burden was not considered.

These cost assumptions were used to calculate the average cost of treating a single phakic eye over 3 years, and a hypothetical cohort of 30 patients with DME and a phakic eye (number based on the cohort of patients reported by Quhill and Beiderbeck [21]). In addition, a breakpoint analysis was performed to illustrate the impact on cost of treating different proportions of patients with continued aflibercept or the FAc intravitreal implant.

3. Results

The cost assumptions in the model and overall calculated costs per eye are detailed in Tables 1 and 2, respectively. An interactive model, which can be tailored to reflect local center treatment pathways, is also available from Alimera Sciences.
3.1. Cost over 3 years per phakic eye

The anticipated total treatment cost per eye in the first year of treatment (including drug and healthcare resource use costs) is £7,665.87 with the current pathway (continued aflibercept monotherapy) and £12,226.68 with the revised pathway (switch to FAc), resulting in additional costs of £4,560.81 in year 1 (Table 2). In subsequent years, however, the anticipated total treatment cost per eye (including drug costs and healthcare resource use) is lower with the revised pathway compared with the current pathway, yielding potential cost savings of £3,211.13 and £2,277.83 in years 2 and 3, respectively (Table 2).

The anticipated total treatment cost per eye over 3 years of treatment (including drug and healthcare resource use costs) is £15,413.23 with the current pathway and £14,485.06 with the revised pathway, resulting in a potential saving of £928.17 on drug and healthcare costs over a 3-year period (Table 2; Figure 2). Over the 3-year period, a total of five clinic visits per patient are freed with the revised pathway (23 vs. 18 visits with the current vs. the revised pathway [Table 3]).

3.2. Cost over 3 years per cohort of 30 phakic eyes in the DME population in England

In a cohort of 30 phakic eyes, the anticipated total treatment cost in the first year of treatment (including drug and healthcare resource use costs) is £229,976.10 with the current pathway and £366,800.40 with the revised pathway, resulting in additional costs of £136,824.30 in year 1 (Table 2). In subsequent years, however, the anticipated total treatment cost per eye (including drug and healthcare resource use costs) is lower with the revised pathway compared with the current pathway, yielding potential cost savings of £96,333.90 and £68,334.90 in years 2 and 3, respectively (Table 2).

In a cohort of 30 phakic eyes, the anticipated total treatment cost per eye over 3 years of treatment is estimated to be £462,396.90 with the current treatment pathway and £434,551.80 with the revised pathway, resulting in a potential saving of £27,845.10 over a 3-year period (Table 2). Over the 3-year period, a total of 150 clinic visits are freed across the study cohort (n = 30) with the revised pathway (690 vs. 540 visits with the current vs. the revised pathway [Table 3]).

A breakpoint analysis illustrating the impact on cost of treating different proportions of patients with continued aflibercept or the FAc intravitreal implant shows that the cost advantage with FAc is maintained when up to 50% of patients receive the FAc implant and the remaining patients receive aflibercept; that is, the total group costs associated with treating up to 50% of patients with the FAc implant are lower than the total group costs associated with treating the remaining patients with aflibercept. The relative cost advantage is lost once at least 60% of patients are treated with the FAc implant; that is, the cost of treating 60% of patients with the FAc implant is greater than the cost of treating 40% of patients with aflibercept (Table 4).

4. Discussion

Anti-VEGF intravitreous injections are the current first-line therapy for patients with DME [6]. While studies have demonstrated the
effectiveness of this therapy in improving visual outcomes over a 3-year period, anti-VEGF injections have been associated with suboptimal response (< 5-letter improvement on the Early Treatment Diabetic Retinopathy Study chart) in around 40% of patients [26]. DME is a multifactorial disease and steroids address its multifactorial nature as they have both anti-inflammatory and anti-VEGF properties [6]. Treatment with the FAc intravitreal implant is based on single-injection technology, which provides an effective therapy, lasting for up to 36 months [14,15,25].

Currently, however, NICE only recommends its use in patients with persistent or recurrent DME and pseudophakic eyes on the grounds that cost-effectiveness has not been demonstrated in patients with phakic eyes [19]. The model reported here indicates that in patients with phakic eyes and DME with a suboptimal response after five initial injections of aflibercept switching treatment to a single FAc intravitreal implant (allowing for a top-up injection of aflibercept in 25% of eyes) can achieve cost savings relative to continued aflibercept. Lower drug costs and fewer clinic visits for treatment and monitoring with the implant relative to continued aflibercept contribute to the overall cost advantage. New treatments for a growing and aging population mean that pressures on the health service are now greater than they have ever been [27]. The fact that fewer clinic visits are required for patients switched to the FAc

**Table 3.** Clinic appointments used.

|                  | Current pathway | Revised pathway | Difference (revised versus current pathway) |
|------------------|-----------------|-----------------|------------------------------------------|
| **No of visits** | **Aflibercept** | **FAc**         |                                          |
| Aflibercept      | 23              | 5               | –18                                      |
| Fluocinolone acetonide implant | 0               | 13              | 13                                       |
| Clinic appointments totals | 23              | 18              | –5                                       |

**Table 4.** Breakpoint analysis to assess the cost of treating varying proportions of DME patients with a phakic lens (n = 30) with continued aflibercept injections and a single FAc intravitreal implant.

| Proportion of patients treated (AFL:FAc), % | AFL | FAc | Dominant treatment\(^b\) |
|-------------------------------------------|-----|-----|-------------------------|
| 100:0                                      | £462,397 | £0 | FAc                     |
| 90:10                                      | £416,157 | £43,455 | FAc | $43,455 | FAc |
| 80:20                                      | £369,918 | £86,910 | FAc | $86,910 | FAc |
| 70:30                                      | £323,678 | £130,366 | FAc | $130,366 | FAc |
| 60:40                                      | £277,438 | £173,821 | FAc | $173,821 | FAc |
| 50:50                                      | £231,198 | £217,276 | FAc | $217,276 | FAc |
| 40:60                                      | £184,959 | £260,731 | AFL | $260,731 | AFL |
| 30:70                                      | £138,719 | £304,186 | AFL | $304,186 | AFL |
| 20:80                                      | £92,479 | £347,641 | AFL | $347,641 | AFL |
| 10:90                                      | £46,240 | £391,097 | AFL | $391,097 | AFL |
| 0:100                                      | £0    | £434,552 | AFL | $434,552 | AFL |

\(^a\)AFL = aflibercept; DME = diabetic macular edema; FAc = fluocinolone acetonide  
\(^b\)Dominant treatment refers to the lowest cost.
intravitreal implant indicates that the revised pathway approach has the potential to address the pressure for clinic appointments.

The model simulates two scenarios: a current and a revised, hypothetical clinical pathway. The model and its assumptions are underpinned by both clinical trial and real-world evidence. Limitations include that the model only evaluates treatment in one eye per patient and does not take into account any impact of bilateral treatment. It also does not take into account retreatment within the anticipated 3-year period. In the FAME trial, 24% of patients received a second FAc intravitreal implant within the 3-year treatment period. In addition, the number of injections included in the model for suboptimally responsive patients receiving aflibercept monotherapy (seven, four, and three injections in years 1, 2, and 3, respectively) may be seen as conservative for this group of patients [14]. The model does also not reflect the costs associated with travel to clinic appointments for patients and carers, or any costs due to the management of the anxiety associated with intravitreal injections. Evidence suggests that, for example, the majority of patients require a carer’s assistance at the time of the injection appointment or time off work for each appointment (at least one day) [28]. Although these costs are not included in the model, reducing the appointment burden would greatly benefit patients [28].

Results from the current analysis are broadly in line with those of a similar cost analysis model developed by Quhill and Beiderbeck, which evaluated the 3-year cost of treating vision impairment associated with persistent or recurrent DME in the NHS in England with either a single FAc intravitreal implant or 14 ranibizumab injections [21]. The model by Quhill and Beiderbeck accounted for the overall direct cost of treatment in both phakic and pseudophakic eyes, including treatment costs (i.e., drug acquisition and administration costs), monitoring costs, the cost of additional interventions required, and the cost of managing adverse events [21]. The model indicated a considerable cost saving with the FAc intravitreal implant, irrespective of lens status, even allowing for the additional cost of cataract surgery in the majority of steroid-treated phakic eye patients, with overall cost savings over the 3-year period of £6,068 per pseudophakic eye and £5,431 per phakic eye [21]. Results are also in line with those reported for a short-term cost comparison in Germany of licensed intravitreal therapies for fovea-involving DME insufficiently responsive to initial anti-VEGF therapy [29]. That cost comparison indicated that steroid implants can provide significant cost savings versus in-label anti-VEGF treatment for center-involving DME (costs with anti-VEGF agents were > 1.5 times higher than those with the FAc implant, which was shown to be the most cost-efficient in-label treatment option [29]).

4.1. Clinical relevance

The first-line therapy for patients with DME is with intravitreal anti-VEGF agents, with or without adjunctive macular laser treatment [6]; however, a significant proportion of patients have persistent or recurrent edema despite repeated anti-VEGF injections [8–12]. Data from Phase III trials (FAME) support the clinical utility of the FAc intravitreal implant in achieving further resolution of edema and improving visual acuity outcomes in this challenging group of patients [14,15,25]. The current cost analysis demonstrates that, over a 3-year period, the use of the FAc intravitreal implant has the potential to be cost saving despite increased upfront costs. Published analyses have also indicated that use of the FAc intravitreal implant can produce a cost advantage, compared with the continued use of anti-VEGF agents [21]. In addition, Mourtoukos et al. note that, in a busy clinical setting with increasing demand for intravitreal therapies, the treatment with the FAc intravitreal implant for persistent or recurrent DME is a suitable and effective option to increase capacity, while also providing an option to reduce the burden on patients and improve their compliance [30]. When comparing the results of switching from anti-VEGF therapy to a single FAc implant with those of continued multiple injections of anti-VEGF monotherapy over a 3-year period, the net advantage for FAc is the reduced number of injections administered by the physician and the reduced number of treatment visits required for the patient (despite allowing for a top-up injection of aflibercept in 25% of eyes each year), which may be of greater value in real terms than the cost advantage.

5. Conclusions

In patients with persistent or recurrent DME in phakic eyes, treatment with the FAc intravitreal implant after an initial suboptimal response to aflibercept is associated with a cost advantage (even when the initial aflibercept cost is included) versus continued treatment with aflibercept injections. In current practice, however, NICE recommends using the FAc implant in patients with persistent or recurrent DME who have a pseudophakic lens. The reality for patients with a phakic lens is, therefore, a scenario where those with a suboptimal response (<5-letter improvement) continue to receive anti-VEGF treatment. The continued use of an anti-VEGF agent has cost implications and only delivers a suboptimal visual acuity response. Data from the current study and published literature indicate that the FAc intravitreal implant has a cost advantage in patients, irrespective of their lens status, and its availability would provide physicians with an alternative treatment option for patients with persistent or recurrent DME in a phakic eye. The true advantage of FAc, however, may be better illustrated by its potential to reduce the treatment burden compared with anti-VEGF treatments.
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