Research Article

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Budget impact analysis of ocriplasmin for the treatment of symptomatic vitreomacular adhesion in the USA

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Background: Vitreomacular traction (VMT) treatment options include watchful waiting, vitrectomy and intravitreal ocriplasmin injection (Jetrea®). This analysis used results from the recently completed OASIS randomized clinical trial to evaluate the 2-year budget impact of ocriplasmin injection availability for treatment of Stage I or II VMT without epiretinal membrane formation in a modeled US health plan. **Materials & methods:** VMT prevalence, treatment patterns and disease resolution rates were from literature, a US retinal-specialist survey and the OASIS trial. Medicare payment rates were applied and a national scenario analysis was conducted. **Results:** With ocriplasmin available, vitrectomy use and complications-related costs decreased. Budget impact of ocriplasmin to the health plan was US$143,599 over 2 years or US$0.0060 per-member per-month. **Conclusion:** Ocriplasmin was projected to be minimally cost-additive at US$0.0060 per-member per-month over 2 years.

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Keywords: pharmacolysis • vitreoretinal adhesion • vitreoretinal traction

As part of the natural aging process, it is normal for the vitreous that fills most of the interior of the eye to shrink and separate from the retina [1,2]. In some patients, the separation is incomplete, resulting in vitreomacular adhesion, where the vitreous remains attached to the macula, which is the portion of the retina responsible for central vision. Traction due to vitreomacular adhesion can lead to a vitreoretinal interface (VMI) disorder with changes to the retinal architecture and impaired vision known as symptomatic vitreomacular adhesion or vitreomacular traction (VMT). Symptoms of VMT can include metamorphopsia (breakup or distortion of the visual image), decreased visual acuity, difficulty in using both eyes together and diplopia (double vision), which interfere with patients' normal daily functioning [3]. Without treatment, patients with earlier stage VMT can progress to the development and expansion of full-thickness macular holes (FTMHs), which are breaks in the macula that disrupt retinal function [2,4]. FTMHs cause severe visual impairment in the central field of vision that interferes with patients' ability to drive or read. As the FTMH enlarges, the probability of successful closure of the FTMH with treatment decreases.

The evaluation of VMI disorders and diagnosis of VMT has improved in recent years with the introduction and increasing adoption of spectral domain optical coherence tomography (SD-OCT) [5]. SD-OCT allows for the imaging of VMI with higher resolution and greater detail than was previously available, thereby enabling improved assessment and diagnosis of VMI disorders. The International Vitreomacular Traction Study (IVTS) classification system for VMI disorders re-evaluated the staging system of VMT and macular holes, defining Stage

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I as VMT without FTMH, Stage II as VMT with small (≤250 μm) to medium (>250 to ≤400 μm) FTMH, Stage III as VMT with large FTMH (>400 μm) and Stage IV as any FTMH without VMT [6]. Without SD-OCT, classification of macular holes into a clinically relevant system would not have been possible.

The American Academy of Ophthalmology's Preferred Practice Pattern® Guidelines have recognized three options for the treatment of VMT and/or FTMH: watchful waiting (observation), vitrectomy (surgical removal and replacement of the vitreous with saline solution) or intravitreal ocriplasmin injection (Jetrea®; ThromboGenics NV, Leuven, Belgium) [3,4]. Complications of vitrectomy can include increased ocular pressure, cataract, retinal break and detachment and endophthalmitis [3,7–11]. As a result, prior to the approval of ocriplasmin, vitrectomy was often delayed despite VMT diagnosis until the symptoms of VMT had progressed sufficiently to warrant the associated risks. In the interim, patients have traditionally been managed under a watchful waiting strategy to monitor for worsening visual impairment.

Ocriplasmin injection is approved in the USA for the treatment of symptomatic vitreomacular adhesion (i.e., VMT) [12]. The recently completed 24-month OASIS randomized clinical trial demonstrated the safety and efficacy of ocriplasmin injection for the treatment of patients with IVTS Stage I or II VMT (i.e., without FTMH or with FTMH ≤400 μm, respectively) without epiretinal membrane (ERM) [13,14]. This trial was consistent with, and expanded on, the results of previous 6-month randomized clinical trials (MIVI-TRUST) by demonstrating safety and sustained improvements in VMT resolution over longer follow-up [15]. Ocriplasmin treatment consists of one injection per patient, and only one course of ocriplasmin treatment may be administered per patient. The proportion of Stage I patients who achieved VMT disease resolution without vitrectomy and the proportion of Stage II patients who experienced nonsurgical FTMH closure without vitrectomy was higher among those treated with ocriplasmin injection compared with those who received a sham injection. However, the cost associated with adopting new interventions like ocriplasmin injection for VMT is a concern as healthcare costs in the USA are rising faster than the gross domestic product [16,17]. US health insurance payors paid US$2.2 trillion in 2014. The net change in costs of adopting new technologies or interventions from various stakeholder perspectives can be evaluated using budget impact analyses [16,18]. In light of the new efficacy data for ocriplasmin injections from the OASIS trial, this study aimed to evaluate the potential net budget impact to a health plan payor of making ocriplasmin injections available for treatment of Stage I or II VMT.

Methods

A budget impact model was developed to assess the potential net change in costs of care for Stage I or II VMT over 2 years due to the availability of ocriplasmin injection to a health plan. As a modeled analysis, this study did not require Institutional Review Board approval. The model was developed and constructed in accordance with the principles of good practice published by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) [18].

Analytical framework

This payor-perspective analysis considered and compared the budget implications of two arms: ocriplasmin injection was not available as a treatment option for Stage I or II VMT (no ocriplasmin) and ocriplasmin injection was available (with ocriplasmin). The budget impact to a hypothetical health plan due to the availability of ocriplasmin injection was assessed as the net difference in direct medical costs between the two arms over 2 years, and assessed using biannual, annual and cumulative 2-year time periods. This time horizon was chosen to reflect the follow-up duration of the OASIS randomized clinical trial. Further, based on clinical expert opinion and previous health technology assessments from NICE, additional treatments for VMT after 2 years are not likely [19]. Total and per-member-per-month (PMPM) budget impacts were both evaluated.

In the two arms, different treatment options were available to the prevalent Stage I and Stage II VMT population at model initiation and to those patients who did not achieve disease resolution (Figure 1). The probabilities of resolution and treatment strategy switching were considered at 6-month intervals.

Patient population

Patients with Stage I or II VMT without ERM were considered eligible for ocriplasmin injection in this analysis based on the OASIS randomized clinical trial patient population [13]. The prevalence of Stage I or II VMT without ERM in the USA was calculated using data from published literature on the Beaver Dam Eye Study. Meuer *et al.* reported that the prevalence of VMT without ERM in the study population was 0.436% based on SD-OCT

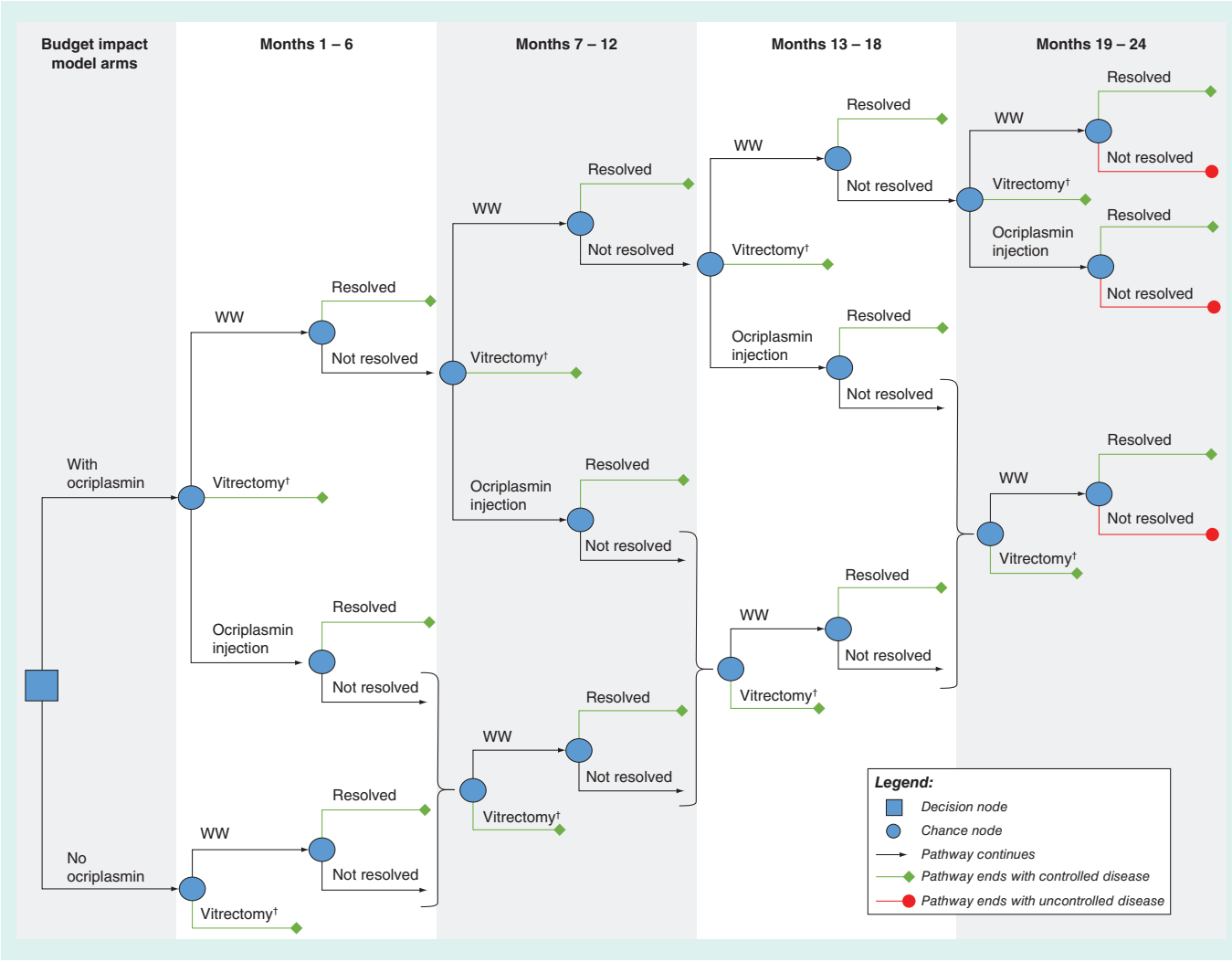

Figure 1. Analytical framework.
†Stage I patients undergoing vitrectomy were assumed to resolve 100% of the time. Stage II patients undergoing vitrectomy were assumed to resolve 95% of the time. Stage II patients who did not resolve had a second vitrectomy 54.5% of the time, with a resolution rate of 47.5%.
WW: Watchful waiting.

scans performed at the 20-year follow-up visit [20]. The age of the study population at that visit ranged from 63 to 102 years.

A previous publication of the Beaver Dam Eye Study by Klein *et al.* demonstrated that the prevalence of visual impairment increases sharply after approximately 60 years of age [21]. Therefore, the prevalence of VMT without ERM reported by Meuer *et al.* was applied to patients 60 years of age or older at base case. The proportion of the population over 60 years of age in this modeled hypothetical health plan was 22.3% based on the US population projections by age for 2018 reported by the US Census Bureau [22]. This results in an all-ages prevalence of VMT without ERM of 0.0971% at base case (Table 1). If the prevalence observed in the Beaver Dam Eye Study was applied to the 16.0% of patients expected to be over 65 years of age, the all-ages prevalence would be 0.0699% while using VMT prevalence rates by age reported in a large study of patients over 45 years of age in Spain resulted in an all-ages prevalence of 0.1607% [20,22,23]. The analysis followed one prevalent cohort over 2 years. Due to the scarcity of data on the incidence of VMT, this analysis did not account for VMT incidence during the time horizon.

Table 1. Analysis parameters.

Input	Base case value	Low	High	Ref.
All ages prevalence of VMT without ERM	0.0971%	0.0699%	0.1607%	[20,22,23]
Proportion of VMT patients who are eligible	94.1%	79.2%	100%	[15,24]
IVTS stage distribution among eligible patients:				[15,24]
– Stage I	84.2%	79.2%	100%	
– Stage II	15.8%	0%	20.8%	
Treatment probabilities†				[25]
Vitrectomy in the 'no ocriplasmin' scenario:				
– Stage I	32.5%	27.8%	42.29%	
– Stage II	100.0%	85.0%	100.0%	
Ocriplasmin injection in the 'with ocriplasmin' scenario:				
– Stage I	14.5%	7.9%	18.7%	
– Stage II	15.0%	4.9%	19.9%	
FTMH closure with vitrectomy				[26]
Probability of success with first vitrectomy	95.0%	91.0%	98.0%	
Probability of second vitrectomy	54.5%	44.7%	64.2%	
Resolution with treatment				[13,14]
Stage I				
Sham:				
– Month 6	12.8%	4.8%	25.7%	
– Month 12	4.9%	2.9%	6.9%	
– Month 18	0.0%	0.0%	0.0%	
– Month 24	2.6%	1.6%	3.6%	
Ocriplasmin injection:				
– Month 6	50.5%	40.1%	60.9%	
– Month 12	10.6%	8.5%	13.0%	
– Month 18	2.4%	2.0%	2.9%	
– Month 24	0.0%	0.0%	0.0%	
Stage II				
Sham:				
– Month 6	11.5%	2.4%	30.2%	
– Month 12	0.0%	0.0%	0.0%	
– Month 18	0.0%	0.0%	0.0%	
– Month 24	0.0%	0.0%	0.0%	
Ocriplasmin injection:				
– Month 6	30.0%	17.9%	44.6%	
– Month 12	0.0%	0.0%	0.0%	
– Month 18	0.0%	0.0%	0.0%	
– Month 24	0.0%	0.0%	0.0%	
Costs per patient				
Physician visit	US$131.76	US$119.96	US$165.18	[27]
Vitrectomy procedure				
Physician fee:				[27,28,29]
– Stage I	US$1086.84	US$995.50	US$1401.96	
– Stage II	US$1177.35	US$1079.19	US$1521.80	
Facility fee:				[28,29,30,31,32,33]
– Stage I	US$2732.45	US$1757.90	US$3997.02	
– Stage II	US$2732.45	US$1757.90	US$3997.02	
– Postprocedure follow-up visits (2×)	US$263.52	US$239.92	US$330.36	[3,4,27]

† Remaining patients are managed with watchful waiting.
ERM: Epiretinal membrane; FTMH: Full-thickness macular hole; IVTS: International Vitreomacular Traction Study; VMT: Vitreomacular traction.

Table 1. Analysis parameters (cont.).

Input	Base case value	Low	High	Ref.
Ocriplasmin injection procedure:				
– Physician	US$104.34	US$95.54	US$134.78	[27,28]
– Facility	US$10.74	US$6.79	US$15.84	[28,30,31,32,33]
– Drug, per injection	US$2444.87	US$2370.40	US$2844.48	[34,35,36]
– Postprocedure follow-up visits (2×)	US$263.52	US$239.92	US$330.36	[3,4,27]
Complications				
Vitrectomy:				[29]
– Stage I	US$2208.22	US$1656.16	US$2760.27	
– Stage II	US$1552.04	US$1164.03	US$1940.05	
– Ocriplasmin injection	US$294.75	US$221.06	US$368.43	[13,14,29]
– Watchful waiting	US$94.82	US$71.11	US$118.52	[13,14,29]

†Remaining patients are managed with watchful waiting.
ERM: Epiretinal membrane; FTMH: Full-thickness macular hole; IVTS: International Vitreomacular Traction Study; VMT: Vitreomacular traction.

IVTS stage distribution was based on the ReCoVit study, which reported the proportions of VMT patients with or without FTMH [15]. The ReCoVit study did not differentiate between Stage II VMT (small-to-medium FTMH [≤400 μm]) and Stage III VMT (large FTMH [>400 μm]), so the distribution of macular holes by size reported by the Cole Eye Institute was applied [24]. Based on these studies, 94.1% of VMT patients are expected to be in Stage I or II, and therefore eligible for ocriplasmin treatment. Of these eligible patients, 84.2 and 15.8% were expected to have Stage I and Stage II disease, respectively. Input ranges were determined by assuming that the patients with VMT and FTMH in the ReCoVit study were all Stage II (high eligibility, low proportion of Stage I) or all Stage III (low eligibility, high proportion of Stage I).

Treatment distributions

The treatment strategies considered in this analysis were watchful waiting, vitrectomy and ocriplasmin injection. For the 'with ocriplasmin' arm, the probability of ocriplasmin use was based on a US retinal specialists survey conducted in November 2014 of treatment practices for VMT patients by stage in the previous 6 months (Table 1; Supplementary Data: Appendix 1) [25]. The surveyed retinal specialists reported that they treated 14.5 and 15.0% of their recent Stage I and Stage II VMT patients with ocriplasmin, and estimated that they would treat 18.7 and 19.9% of their future Stage I and Stage II VMT patients with ocriplasmin. Among retinal specialists not currently using ocriplasmin, self-reported estimates of future ocriplasmin use were 7.9% for Stage I patients and 4.9% for Stage II patients. These future use estimates were used to inform likely ranges for the uptake of ocriplasmin injection. The probabilities of watchful waiting or vitrectomy among Stage I patients were also based on the survey of retinal specialists. At base case, patients with Stage II VMT (with FTMH ≤400 μm) were not expected to be treated with watchful waiting based on expert opinion. For the 'no ocriplasmin' arm, the probability of any treatment strategy involving ocriplasmin was set to 0 and the probabilities of watchful waiting or vitrectomy were readjusted proportionally to sum to 100%. Alternatively, scenarios were tested assuming that the survey-reported ocriplasmin-treated patients would be treated with all vitrectomy or all watchful waiting in the absence of ocriplasmin.

The 'no ocriplasmin' and 'with ocriplasmin' treatment distributions were applied on a semi-annual basis to patients with unresolved disease in the corresponding comparator arm (Figure 1). Since ocriplasmin injection treatment is intended to be used only once in a given patient, the 'no ocriplasmin' treatment distribution was also applied to patients who were previously treated with ocriplasmin injection in the 'with ocriplasmin' arm.

Disease resolution

All patients with Stage I VMT who underwent vitrectomy were assumed to achieve disease resolution. Stage II VMT patients were expected to achieve disease resolution (macular hole closure) 95% of the time with vitrectomy based on surgical studies (Table 1) [4]. In the event of a failed vitrectomy, 54.5% of patients were expected to undergo a second vitrectomy within 6 months based on expert opinion, consistent with previously published economic analyses [26].

Table 2. Disease resolution rates.

Patients	Watchful waiting			Ocriplasmin injection		
	n	%	95% CI	n	%	95% CI
Stage I VMT, no FTMH:†						
– Total n	47			95		
– Month 6	6	12.8	4.8–25.7%	48	50.5	40.1–60.9%
– Month 12	8	17.0	7.6–30.8%	53	55.8	45.2–66.0%
– Month 18	8	17.0	7.6–30.8%	54	56.8	46.3–67.0%
– Month 24	9	19.1	9.1–33.3%	54	56.8	46.3–67.0%
Stage II VMT with FTMH (≤400 μm):‡						
– Total n	26			50		
– Month 6	3	11.5	2.4–30.2%	15	30.0	17.9–44.6%
– Month 12	2	7.7	0.9–25.1%	15	30.0	17.9–44.6%
– Month 18	2	7.7	0.9–25.1%	15	30.0	17.9–44.6%
– Month 24	2	7.7	0.9–25.1%	14	28.0	16.2–42.5%

Data from the OASIS randomized clinical trial of ocriplasmin injection versus sham treatment for patients with Stage I or II VMT (full analysis set population) [13,14]. Disease resolution defined as pharmacological resolution without vitrectomy for Stage I patients, and as nonsurgical FTMH closure without vitrectomy for Stage II patients.
†$p < 0.001$ for all time points comparing sham versus ocriplasmin injection.
‡p-value nonsignificant for all time points comparing sham versus ocriplasmin injection.
FTMH: Full-thickness macular hole; VMT: Vitreomacular traction.

The rates of disease resolution with the ocriplasmin injection and watchful waiting treatment strategies were based on the results of the OASIS clinical trial in the ocriplasmin- and sham-treatment arms, respectively (Table 2) [13,14]. Disease resolution was defined as pharmacological VMT resolution without vitrectomy for patients with Stage I VMT and as nonsurgical FTMH closure without vitrectomy for patients with Stage II VMT. Increases in disease resolution rates recorded at 6, 12, 18 and 24 months post-treatment initiation in the OASIS trial were applied in this analysis (Table 1) [13,14].

Treatment costs

The analysis considered costs to the payor and all costs are reported in 2018 US dollars. Costs were included for physician office visits, physician and facility procedure fees, drug acquisition and treatment-related complications. Total costs per treatment strategy were US$226.58 for 6 months of watchful waiting, US$3249.98 for ocriplasmin injection, US$6422.79 for a vitrectomy for a patient with Stage I (no FMTH) disease and US$5857.12 for a vitrectomy for a patient with Stage II (with FTMH ≤400 μm) disease.

Treatment administration

Payment schedules for 2018 published by the Centers for Medicare and Medicaid Services (CMS) were used to inform costs in this analysis for physician office eye visits, vitrectomy procedures and ocriplasmin injection drug acquisition and administration (Table 1) [27,30,31,34]. For physician and facility fees, national payment amounts were applied at base case and input ranges were defined using payment amounts for different Medicare Administrative Contractor localities and providers in the USA [27,31–33]. Patients who underwent vitrectomy or ocriplasmin injection were assumed to have two follow-up physician office eye visits based on the minimum follow-up schedule recommended by the American Academy of Ophthalmology Preferred Practice Patterns® Guidelines [3,4].

The drug cost of ocriplasmin was based on average sales price per unit reported by CMS at base case [34]; alternatively, wholesale acquisition cost and average wholesale price per vial from RED BOOK were also tested [35]. Each ocriplasmin injection required three CMS billing units of drug (each billing unit is 0.125 mg; one vial of ocriplasmin contains three units), based on the ocriplasmin injection coding and billing guideline [36]. The patient copayment for drugs was 20%, based on the CMS rate [37].

The distributions of settings of care for ocriplasmin injections or vitrectomies were extracted from the CMS 2016 Physician/Supplier Procedure Summary Master File [28]. The distributions of vitrectomy procedure types performed for VMA/VMT or macular hole reasons in 2009–2010 were extracted from an analysis of the 2008–2012 CMS Outpatient and Carrier (Part B) 5% Standard Analytical Files (SAF) [29]. In accordance with ISPOR guidelines for budget impact models, future costs were not discounted to present value in the base case analysis.

Complication costs

Complication costs following vitrectomy were evaluated using the CMS 2008–2012 Outpatient and Carrier (Part B) 5% SAF (Table 1; Supplementary Data: Appendix 2). The per-patient incidence of common vitrectomy-associated complications and average cost per complication to the payor for up to 2 years postvitrectomy were extracted. Costs were adjusted to 2018 US dollars using the consumer price index for medical care services published by the US Bureau of Labor Statistics [38].

To calculate the average total cost of complications with ocriplasmin injection or watchful waiting, the costs per complication were applied to the probability of treatment-related adverse events in the study eye reported in the OASIS randomized clinical trial among ocriplasmin- or sham-treated patients who had not undergone vitrectomy (Supplementary Data: Appendix 2) [13,14]. These included potential signs of disease progression such as macular hole, retinal detachment and retinal tear. It was assumed that the cost to address a type of complication did not vary based on whether the complication was secondary to vitrectomy, watchful waiting or ocriplasmin. Costs related to serious adverse events observed in the OASIS trial were based on the costs per adverse event found in the analysis of complications following vitrectomy in the CMS 5% SAF. Other serious adverse events were costed as an additional physician office eye visit per event.

Previous ocriplasmin injection clinical trials have found that related adverse events are largely transient [39]. To account for nonserious adverse events, the cost of an additional physician office eye visit was applied to the proportion of patients in the ocriplasmin or sham treatment arms of the OASIS trial who experienced at least one treatment-related adverse event in the study eye, regardless of severity (Supplementary data: Appendix 2) [13,14]. Though cataract was not considered a serious adverse event by the OASIS study investigators, additional costs to treat cataract complications were also included based on the analysis of vitrectomy complications in the CMS 5% SAF.

Scenario analyses

Scenarios in which individual parameter values were changed from base case were used to assess the results given likely alternative parameter values in accordance with ISPOR guidelines [40]. One-way sensitivity analyses were used to assess the variation in model results given input uncertainty by varying the parameter values individually and independently across likely ranges and distributions. With the exception of complications costs, which were varied by ±25% due to lack of other data, all input ranges were based on alternate data sources or assumptions as described. Annual time preference discount rates up to 5% were evaluated in the one-way sensitivity analysis. Resolution rates over time with ocriplasmin injection or watchful waiting were varied as a group for each VMT stage and treatment type across their 95% CIs from the OASIS trial results [13]. The most influential parameters were identified as those whose variations produced the largest magnitude of change in the PMPM budget impact in the one-way sensitivity analyses.

Budget impact was also evaluated in a scenario analysis on the national level using a published threshold from the Institute for Clinical and Economic Review [16]. The population of the health plan was set equal to the projected 2016 US population, patient copay was set to 0% and the total budget impact was compared with the US$452 million threshold for average annual cost growth due to a drug from the published framework [16,22]. Cost impact was also evaluated per capita and per capita per annum in this scenario.

Results

The availability of ocriplasmin injection for the treatment of Stage I or II VMT over a 1-million-member plan was estimated to lead to a cumulative budget impact over 2 years of US$143,599 or US$0.0060 PMPM (Table 3). Of this, Stage I patients accounted for US$112,179 or US$0.0047 PMPM (78.1%), and Stage II patients accounted for US$31,420 or US$0.0013 PMPM (21.9%) (Table 4). Ocriplasmin was cost additive in the first year, then cost saving in the second year for Stage I patients. Stage II patients were not expected to be managed with watchful waiting, so all costs for these patients were incurred in the first year.

VMT prevalence

In a 1-million-member health plan, 971 patients were expected to have VMT without ERM. Of those, 769 were expected to have Stage I disease (VMT without FTMH) and 145 were expected to have Stage II disease (VMT with FTMH ≤400 μm), for a total expected ocriplasmin-eligible population of 914 patients.

Table 3. Cumulative treatment use and budget impact: base case analysis.

Result	Analysis comparator arms		Change
	No ocriplasmin	With ocriplasmin	
Treatments over 2 years[†]			
Patients with watchful waiting only	214	138	-75
Vitrectomies, total:	704	612	-92
– First 6 months	399	340	-59
– After 6 months of watchful waiting	306	201	-105
– After ocriplasmin injection	0	71	71
Ocriplasmin injections	0	238	238
Cumulative costs over 2 years			
Complications-related	US$1,567,336	US$1,421,090	-US$146,248
Total by treatment type:			
– Watchful waiting	US$261,395	US$221,121	-US$40,275
– Vitrectomy	US$4,440,038	US$3,850,731	-US$589,307
– Ocriplasmin injection	US$0	US$773,180	US$773,180
Total	US$4,701,434	US$4,845,032	
Cumulative budget impact			US$143,599[‡]
Budget impact per member per month:			
– Over 2 years			US$0.0060[‡]
– Year 1			US$0.0147
– Year 2			-US$0.0028
– Months 1–6			US$0.0087
– Months 7–12			US$0.0208
– Months 13–18			-US$0.0012
– Months 19–24			-US$0.0043

[†]Some patients may have more than one treatment due to the possibility of second vitrectomy after an unsuccessful first vitrectomy among Stage II patients, or vitrectomy after failing to resolve with ocriplasmin injection.
[‡]Overall budget impact results over the 2-year model horizon.

Table 4. Budget impact by time period and patient group.

Time period	Stage I patients		Stage II patients		All patients	
	Total	PMPM	Total	PMPM	Total	PMPM
Months 1–6	US$112,437	US$0.0187	-US$60,161	-US$0.0100	US$52,276	US$0.0087
Months 7–12	US$33,129	US$0.0055	US$91,581	US$0.0153	US$124,709	US$0.0208
Months 13–18	-US$7314	-US$0.0012	US$0	US$0	-US$7314	-US$0.0012
Months 19–24	-US$26,073	-US$0.0043	US$0	US$0	-US$26,073	-US$0.0043
Year 1	US$145,566	US$0.0121	US$31,420	US$0.0026	US$176,985	US$0.0147
Year 2	-US$33,387	-US$0.0028	US$0	US$0	-US$33,387	-US$0.0028
Cumulative	US$112,179	US$0.0047	US$31,420	US$0.0013	US$143,599	US$0.0060

PMPM: Per member per month.

Treatments used

92 fewer vitrectomies were expected over 2 years with ocriplasmin available than without (Table 3). Decreased vitrectomies were projected among both Stage I and Stage II patients (86 fewer and seven fewer vitrectomies, respectively). Over half of the overall reduction in vitrectomies was expected in the first 6 months.

After the first 6 months, fewer vitrectomies were expected in the 'with ocriplasmin' arm compared with the 'no ocriplasmin' arm for Stage I patients who did not achieve disease resolution under watchful waiting. Stage II patients were not expected to be managed with watchful waiting. This decrease was partially offset by vitrectomies subsequent to ocriplasmin injection in the 'with ocriplasmin' arm among Stage I and Stage II patients. Fewer patients in the 'with ocriplasmin' arm than in the 'no ocriplasmin' arm were expected to be managed with watchful waiting only (no vitrectomy or ocriplasmin injection) over the 2-year time horizon.

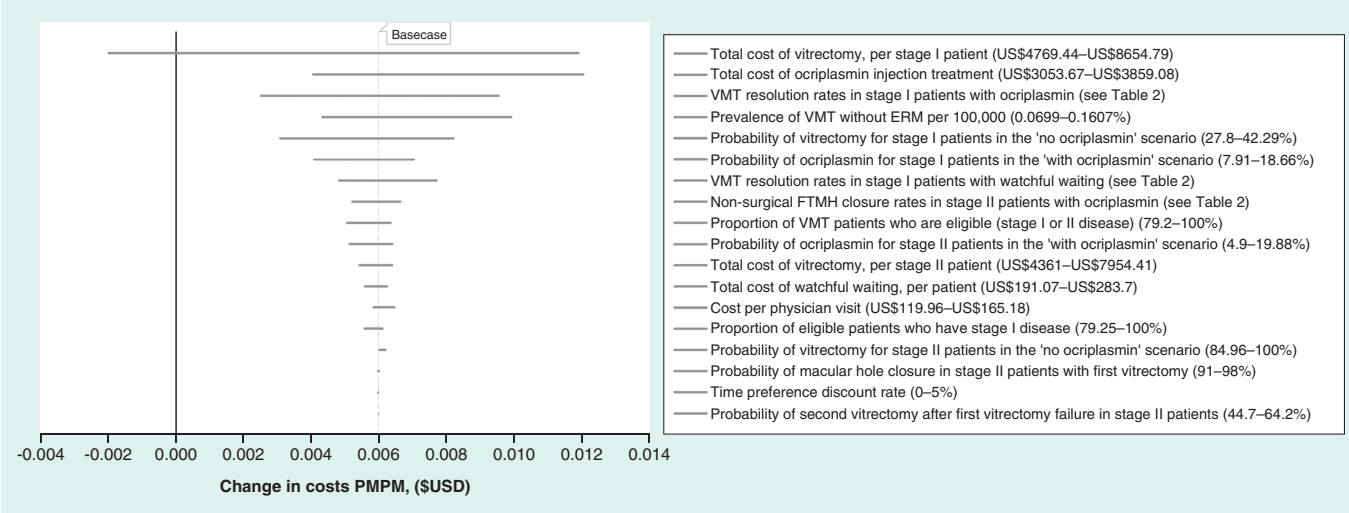

Figure 2. Per-member-per-month budget impact tornado diagram.
ERM: Epiretinal membrane; FTMH: Full-thickness macular hole; PMPM: Per-member per-month; VMT: Vitreomacular traction; USD: United States dollar.

Total treatment costs & complication costs

Less watchful waiting and fewer vitrectomies led to related savings in the 'with ocriplasmin' arm compared with the 'no ocriplasmin' arm (Table 3). This offset the increase in total costs for ocriplasmin injections in the 'with ocriplasmin' arm. Complication costs overall were expected to be lower in the 'with ocriplasmin' arm compared with the 'no ocriplasmin' arm.

Scenario analyses

The PMPM budget impact was most sensitive to variation in the total cost of vitrectomy for patients with Stage I VMT, followed by the total cost of treatment with ocriplasmin injection, VMT resolution rates with ocriplasmin for patients with Stage I VMT and the prevalence of VMT without ERM (Figure 2). The highest PMPM results were observed when the total cost of vitrectomy for Stage I patients was low, or the total cost of ocriplasmin injection was high (US$0.0119 and US$0.0120 PMPM, respectively). One-way sensitivity analyses showed cost savings when the total cost of vitrectomy for a Stage I patient was greater than US$8099. In a separate scenario analysis of the national budget impact, plan size was increased to the projected 2018 US population and patient copay decreased to 0%, and the resulting total budget impact was US$95.2 million or US$0.2890 per capita (US$0.1445 per capita per annum).

Discussion

The net budget impact to a million-member health plan expected with the availability of ocriplasmin injection for the treatment of Stage I or II VMT was US$143,599 over 2 years. The increase in costs for the ocriplasmin injections was partially offset by decreases in costs for other treatment strategies. Over 2 years, the PMPM budget impact was US$0.0060, indicating that ocriplasmin is expected to be minimally cost additive to US health plans.

The bulk of the cost offset was due to reduced vitrectomies; there were 92 fewer vitrectomies expected in the 'with ocriplasmin' arm than in the 'no ocriplasmin' arm. The number of vitrectomies in the first 6 months decreased by 59 and the number after watchful waiting decreased by 105, offsetting the 71 vitrectomies performed after ocriplasmin injection. The costs related to complications were expected to be lower in the 'with ocriplasmin' arm compared with the 'no ocriplasmin' arm, reflecting the reduced risks of costly adverse events with ocriplasmin injection compared with vitrectomy. These results suggest that the minimally cost-additive budget impact of ocriplasmin injection may be due to partial cost offsets from its improved effectiveness over watchful waiting and improved safety profile compared with vitrectomy.

In the national level scenario analysis, the 2-year total budget impact in the USA was projected to be US$95.2 million or US$0.2890 per capita and US$0.1445 per capita per annum. This is far below the US$452 million annual threshold for average cost growth due to a drug published by the Institute for Clinical and Economic

Review [16]. This threshold was set to evaluate whether the cost growth would contribute to a rate of increase in national healthcare costs greater than the rate of increase in US gross domestic product. Thus, the budget impact of ocriplasmin injection was not expected to contribute to overinflated healthcare spending on the US national level.

The analysis was limited by the scarcity of data on the epidemiology of VMT. In particular, there is little data on the incidence of VMT. Many earlier studies of VMT prevalence or retrospective studies of VMT patients relied on diagnoses that were not confirmed via SD-OCT scans. As a result, the current analysis was conducted on a prevalent cohort over 2 years and newly incident patients in the second year were not considered. The size and influence of an incident cohort on the budget impact is unknown. Further, real-world data on the distribution of treatments used to treat VMT were not available. Instead, the treatment patterns for VMT used in this analysis were informed by a survey of practicing clinicians and expert opinion. Even so, none of the scenarios tested in the one-way sensitivity analysis found cumulative results greater than US$0.0120 PMPM. As SD-OCT is increasingly used to diagnose VMT, new research on the epidemiology and treatment patterns for VMT would be useful to support an increased understanding of this disorder and its treatment.

Economic evaluations of treatment options for symptomatic vitreomacular adhesion (i.e., VMT) and macular holes have been published previously. These budget impact analyses of ocriplasmin injection suggested that it may be cost saving in Spain and the Canary Islands (though uncertainty was high) and cost additive in Ireland [41]. The uncertainty of results was attributed to uncertainty in, and model sensitivity to, the costs of ocriplasmin injection and vitrectomy. The US budget impact analysis presented here was similarly sensitive to these costs. However, the US cost inputs were extracted from published CMS fee schedules and analyses of real-world CMS claims data, and one-way sensitivity analyses using published ranges of procedure payment rates did not return cumulative results greater than US$0.0120 PMPM.

A review of economic studies of ocriplasmin injection reported that ocriplasmin has been found to be a cost-effective treatment for VMT patients without ERM in Canada, France and the UK compared with watchful waiting followed by vitrectomy as needed [41]. Results were less positive in unselected VMT populations with ERM. In the USA, a previously published cost–effectiveness analysis evaluated three treatment scenarios: vitrectomy, ocriplasmin injection and saline injection [42]. Saline injection was used as the control in the MIVI-TRUST studies [15], and the results among these patients were used to inform the disease management arm without active treatment in the model. Vitrectomy and ocriplasmin injection were both cost-effective compared with no active treatment in this unselected VMT population including patients with ERM, demonstrating cost–effectiveness ratios well below the US$50,000 per quality-adjusted life year threshold widely used as a benchmark in the USA. Unlike the ex-US studies, cost–effectiveness in the USA for the non-ERM subgroup was not evaluated separately.

Inputs for the US budget impact analysis presented here differ from those used in the previously published US cost–effectiveness analysis [42]. In particular, this budget impact analysis was conducted on the ERM-negative subgroup of the VMT population. This subgroup of the approved indication for ocriplasmin has been shown in previous randomized clinical trials to be associated with higher resolution rates. The efficacy of ocriplasmin injection for VMT patients with or without FTMH in the previously published US cost–effectiveness analysis was based on the 6-month MIVI-TRUST studies including ERM patients, while the US budget impact analysis presented here used results from the recently-completed 24-month OASIS clinical trial of ERM-negative VMT patients.

Conclusion

This budget impact model found that ocriplasmin injection for treatment of Stage I or II VMT without ERM is minimally cost additive at US$0.0060 per member per month. Cost offsets included an expected reduction in the number of vitrectomies and complication-related costs overall. Future research on the cost–effectiveness of ocriplasmin injections in VMT patients without ERM based on the newest clinical trial data will be useful to improve the understanding of the economic impact of ocriplasmin injection in the USA.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: https://www.futuremedicine.com/doi/suppl/10.2217/cer-2018-0057

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Summary points

- Without effective treatment, vitreomacular traction (VMT) can lead to the development of holes in the macula of the eye, causing severe impairment to patients' vision and function.
- Ocriplasmin injection offers a less invasive active treatment option than vitrectomy surgery for patients with Stage I to II VMT (with or without a small-to-medium full-thickness macular hole), particularly those without epiretinal membrane (ERM).
- The 24-month OASIS randomized clinical trial demonstrated that ocriplasmin injection for Stage I to II VMT patients without ERM improved disease resolution.
- This budget impact model found that ocriplasmin for Stage I to II VMT patients without ERM was expected to be minimally cost additive on average over 2 years to the health plan (US$0.0060 per member per month), and cost saving in the second year (-US$0.0028 per member per month).
- The availability of ocriplasmin injection treatment was expected to reduce the number of more invasive vitrectomy surgical treatments for both Stage I and Stage II VMT patients.
- Costs related to VMT treatment complications were expected to decrease with the ocriplasmin injection treatment option available.

Data sharing statement

The authors certify that this manuscript reports the secondary analysis of clinical trial data that have been shared with them and that the use of this shared data is in accordance with the terms (if any) agreed upon their receipt. The source of this data is: the OASIS trial (NCT01429441).

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