



Published in final edited form as:

Ophthalmology. 2016 March ; 123(3): 497–504. doi:10.1016/j.ophtha.2015.10.043.

Surgical versus medical treatment of ocular surface squamous neoplasia: A cost comparison

Christina S. Moon, MD¹, Afshan A. Nanji, MD, MPH¹, Anat Galor, MD, MSPH^{1,2}, Kathryn E. McCollister, PhD³, and Carol L. Karp, MD¹

¹Bascom Palmer Eye Institute, University of Miami, Miami, Florida

²Miami Veterans Affairs Medical Center, Miami, Florida

³Department of Public Health Sciences, University of Miami, Miami, Florida

Abstract

Purpose—The objective of this study was to compare the cost associated with surgical versus interferon (IFN α 2b) treatment for ocular surface squamous neoplasia (OSSN).

Design—A matched, case-control study.

Participants—Ninety-eight patients with OSSN; 49 of whom were treated surgically and 49 of whom were treated medically.

Methods—Patients with OSSN treated with IFN α 2b were matched to surgery patients based on age and date of treatment initiation. Financial cost to the patient was calculated using two different methods (hospital billing and Medicare allowable charges) and compared between the two groups. These fees included physician fees (clinic, pathology, anesthesia, and surgery), facility fees (clinic, pathology, and operating room), and medication costs. Time invested by patients was calculated in terms of number of visits to the hospital and compared between the two groups. Parking costs, transportation, caregiver wages, and lost wages were not considered in our analysis.

Main outcome measures—Number of clinic visits and cost of therapy as represented by both hospital charges and Medicare allowable charges.

Results—When considering cost in terms of time, the medical group had an average of 2 more actual and imputed number of visits over 1 year compared to the surgical group. Cost as represented by hospital charges was higher in the surgical group (mean \$17,598, SD \$7,624) when compared to the IFN α 2b group (mean \$4,986, SD \$2,040). However, cost between the two groups was comparable when calculated based on Medicare allowable charges (surgical group: mean \$3,528, SD \$1,610; medical group: mean \$2,831, SD \$1,082; $P = 1.00$). The highest cost category

Correspondence: Carol L. Karp, MD Bascom Palmer Eye Institute University of Miami Miller School of Medicine, 900 NW 17th Street, Miami, FL 33136, ckarp@med.miami.edu.

Presented as a poster at the American Academy of Ophthalmology 10/20/14

Conflict of interest: None

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

in the surgical group was the excisional biopsy (Hospital billing \$17,598; Medicare allowable \$3,528) while the highest cost in the medical group was interferon (\$1,172 for drops, average 8.0 bottles; \$370 for injections, average 5.4 injections).

Conclusion—Our data in this group of patients previously demonstrated equal efficacy of surgical versus medical treatment. Here, for the first time, we consider costs of therapy and found that medical treatment involved slightly more office visits whereas surgical treatment could be more or equally costly depending on insurance coverage.

Introduction

Ocular surface squamous neoplasia (OSSN) is an umbrella term for a spectrum of epithelial dysplasia of the conjunctiva and cornea ranging from epithelial dysplasia to carcinoma in situ to invasive squamous cell carcinoma.¹ The current mainstay of therapy is surgical excision with a “no-touch technique”² and with cryotherapy to conjunctival margins.³ However, surgical therapy can be associated with significant limbal stem cell deficiency, infection, induced astigmatism, diplopia, and symblepharon.

As such, given the potential side effects of surgical treatment and increasing evidence that topical therapies are effective in the treatment of OSSN, more providers⁴ are opting for the use of topical therapies. Advantages of topical therapy include the ability to treat the whole ocular surface and to avoid morbidity associated with large excisions. The most commonly used agents are interferon-alpha 2b,^{5–12} 5-FU (5-fluorouracil)^{13–16}, and mitomycin-C.^{17–22} Our practice favors interferon alpha-2b eye drops, as the side effect profile is the mildest.¹⁴

While there is increasing evidence that interferon alpha-2b is an effective treatment for OSSN,^{5, 7, 23} there is a knowledge gap regarding the time and financial cost of a surgical approach compared to medical treatment. Our group recently published that a cohort of patients receiving surgical treatment and a cohort of patients receiving medical treatment had no significant differences in side effects, complications, or recurrences.²³ We now take the analysis a step further in the same cohort of patients with OSSN (Table 1) to compare the cost associated with these two modalities.

Methods

Study population

This study was approved by the institutional review board of the University of Miami. The design was a retrospective, matched, case-control study. For the medical arm of the study, patients treated with IFN α 2b were selected by a screening of the Bascom Palmer Eye Institute (BPEI) pharmacy database. OSSN patients were included if they were successfully treated with IFN α 2b as the primary treatment. Exclusion criteria for the medical arm of the study included patients treated with IFN α 2b adjuvantly for positive margins after surgery or if they failed primary treatment. Of the 61 patients identified, 49 met the criteria for inclusion. Of the 12 excluded patients, 6 failed treatment with interferon or were lost to follow up prior to resolution, 3 used interferon for treatment of positive surgical margins, 2 were unable to tolerate interferon and preferred excision, and 1 had been started on interferon by a referring ophthalmologist but with an unclear diagnosis. In order to select the

matched cases for the surgical arm of the study, the Florida Lions Eye Bank pathology database, which contains over 500 patients with excisional surgery as the primary treatment for OSSN was screened. Matches were created based on patient age (within 10 years) and date of surgical excision (within 10 years). Surgically matched patients were treated successfully with surgery only; patients treated with adjuvant medical therapy after their surgeries were not eligible for matching.

Surgically treated group

Excisional biopsy was performed in the setting of the operating room at Bascom Palmer Eye Institute in Miami (n= 43), in the ambulatory surgical center at Bascom Palmer Eye Institute in Palm Beach Gardens (n=2), in the Minor Procedure Room at Bascom Palmer Eye Institute in Miami (n=2), or in the clinic at Bascom Palmer Eye Institute in Miami (n=2). Eleven providers performed the excisional biopsies. Surgical treatment consisted of lesion excision with up to 4 mm of tumor-free conjunctival margins excluding the limbal margin (mean 2.7mm for those with known margin width, n=34). Cryotherapy was applied to the limbus and conjunctival edges in a double freeze-thaw method in 41 of the excisions, intra-operative mitomycin C was applied in one case, and sclerectomy was performed in six cases. Amniotic membrane was used to cover the area of excision in 14 cases, conjunctival autograft in one case, primary closure in ten cases, and the rest were left open with bare sclera. Pathology to identify the lesion as an OSSN was performed by one of two experienced ocular pathologists at the Bascom Palmer Eye Institute.

Medically treated group

Patients were treated with IFN α 2b in the form of drops (n =40), subconjunctival/perilesional injections (n=1) or combination drop and injection therapy (n=8). A dose of 1 million IU/mL (n=35) or 3 million IU/mL (n=11; n=2 for combination of doses) was used for topical therapy. A dose of 3 million international units (in 0.5 ml) was used for subconjunctival injections. Eye drops were administered with an initial dose of 4 times daily (with one exception of 3 times daily) until clinical resolution.. Patients were initially seen on a monthly basis to assess treatment response, with a gradual lengthening of follow up time to every 2 to 3 months. Duration of interferon therapy was based on treatment response.

Main outcome measures

Our two main outcome measures were time considerations and financial cost incurred with each treatment modality. With regards to time, the number of visits was tallied from the initiation of interferon or surgery for one year thereafter. With respect to the financial cost, costs were calculated using two different methods (Table 1.) The first cost estimation was of hospital billing charges (at 2013 prices) while the second estimation was of the reimbursements based on Medicare allowable. Medicare allowables were calculated using the 2013 Medicare fee schedules acquired from the Centers for Medicare and Medicaid Services (CMS) specific to a hospital-based practice in the geographic area of Miami, FL, and also for an ASC in the same geographic area. More detailed information about financial costs is described below.

Hospital billing information

Excisional biopsy—To determine the financial billing charges of an excisional biopsy in the operating room, full billing records were obtained in 40 patients detailing the itemized facility fee, the surgeon fee, and the anesthesia/nurse anesthetist fee for the procedure. Billing records included 3 costs: physician charge, facility fee, and anesthesia costs. Of those, physician and anesthesia costs were stable over the years. The facility fee included several itemized fees including all materials used during the procedure (including amniotic membrane, if used, as well as fees for the use of surgical and anesthesia equipment. Of those, the cost of most items remained stable over the study period with the exception of the charge for the use of the holding area, the charge for the hourly use of the operating room, the charge for the hourly use of anesthesia equipment, and the charge for the use of amniotic membrane. These prices were all adjusted to reflect 2013 itemized charges for these items at Bascom Palmer Eye Institute.

Two cases were performed in the minor operating room (OR). In these cases, charges were calculated based on 2013 charging schedules for use of the minor OR facility and physician fees for biopsy. An additional two patients had lesions small enough to be excised in the clinic. For these patients, 2013 prices for in office facility and physician fees were applied. In 5 patients, billing records were incomplete. In these cases, we did have complete surgical, nursing, and anesthesia notes from which we were able to calculate surgical time, anesthesia time, and the cost of materials. These records were used to impute the missing values, itemized facility fees, and confirm the CPT procedure code that was billed at the time of surgery. For the physician charges and fees, the costs were calculated based on the procedure codes used. For the anesthesia (anesthesiologist and/or nurse anesthetist) and facility costs, expenses were calculated by imputing values based on surgical time and procedure codes. The charges for pathology were calculated using 2013 charges.

Incisional (in office) biopsy and pathology charges—The charges for in-office incisional biopsies (29 in the IFN group and 2 in the excisional group) were calculated using 2013 charges for facility and physician fees. (Table 1) The charges for pathology were calculated using 2013 charges for facility and physician fees.

Hospital visits—Visits for surgical patients were separated into visits within the first 3 months (the global period for post-operative care) and visits within the first year. No global period was used for excisional biopsies performed in the clinic or minor operating room. To determine the financial costs of visits, it was assumed that initial visits were billed as Level 3, new patients and that subsequent visits were billed as Level 3, established patients. Patients with less than 1 year of follow-up had visits imputed based on the routine follow-up schedule. In the surgical group, the day of surgery was counted as the first visit to the hospital. Then, patients were seen 4 times in the first three months after surgery (1 day, 1 week, 1 month, 3 months) and then every 3 months for the remaining year. In this group, only visits that occurred after the 90 day global period were included in the cost analysis. For the medical group, patients were typically seen monthly until tumor resolution, after which follow-up was every 3 months in the first year.

Medications—The billing of medications was calculated using 2013 prices of medications at the Bascom Palmer pharmacy. (Table 2) Patient operative reports and clinical records were reviewed to determine the type and duration of medications used. Medications were included in our analysis if the reason for use was directly related to surgical or medical treatment. For example, in surgical patients on topical steroids during the postoperative period, glaucoma medications were used by providers if they developed an increase in intraocular pressure thought to be a steroid response. The duration of treatment was used to estimate how many bottles/tubes a patient would have purchased. For ointment, it was assumed that one 3.5 g tube of ointment would last approximately 3 weeks. For drops, it was assumed that there were 20 drops present in 1 mL and the number of bottles was estimated using information on frequency and duration of use. For example, a 3 mL bottle of interferon would have 60 drops present in the bottle, and with four times a day dosing would be estimated to last 15 days. A 3 mL bottle of interferon 1 million units per millimeter cost \$130 and was estimated to last 15 days and a 3 mL bottle of interferon 3 million units per millimeter cost \$180 per bottle and was estimated to last 15 days. Interferon injections of 3 million units per 0.5 millimeters cost \$68 per injection.

Medicare allowable method

Excisional biopsy

Physician reimbursements were calculated using 2013 Medicare fee schedules²⁴ specific to a hospital-based practice in the geographic area of Miami, FL.²⁵ In this fee schedule, physician work RVUs, or relative value units, are units based on the relative amount of time, technical skill, and effort required by a physician to provide a service. Each CPT (current procedural terminology) code has a relative value associated with it that is multiplied by a conversion factor and a geographical adjustment.²⁶ The dollars per RVU (relative value unit) value used was \$34.023, the established rate for 2013. When more than 1 CPT code was used, the highest valued procedure was calculated at 100% of the fee schedule and thereafter the physician fees were calculated at 50% of the fee schedule. Reimbursement for unlisted codes was estimated based on reimbursement data determined by Medicare adjusters for the year 2013 for similar surgeries.

Facility fee reimbursements were calculated similarly to the physician fee reimbursements using 2013 Medicare fee schedules²⁷ specific to a hospital based practice in the geographic area of Miami, FL²⁸ and an ambulatory surgical center in Palm Beach, FL for the cases done there.²⁵

Anesthesia professional fees were calculated based on the sum of base units (determined by the type of surgical procedure) and time units (in units of 15 minutes), multiplied by the conversion factor 25.52, specific to a hospital-based practice in the geographic area of Miami, FL.²⁹ CPT code 00140, anesthesia for conjunctival surgery is weighed as 5 base units. One time unit is 15 minutes and the cases were estimated as either 4 time units (1 hour) or 6 time units (1.5 hours) based on anesthesia time recorded in hospital records. Thus, anesthesia professional fee reimbursements for surgeries were either \$229.68 (1 hour) or \$280.72 (1.5 hours).

Incisional (in office) biopsy and pathology costs

The reimbursements for in-office biopsies were calculated using the 2013 Medicare fee schedules acquired from the Centers for Medicare and Medicaid Services (CMS) specific to a hospital-based practice in the geographic area of Miami, FL. Reimbursements were calculated as equal between the surgical group and those in the medical group who received biopsies for pathology, which was calculated using the 2013 Medicare fee schedule.

Clinic visits and medications

Reimbursements for clinic visits and medication costs were calculated using the same assumptions that were used to calculate costs in the hospital billing information above.

Statistical analysis

Statistical analyses were performed using the SPSS 20.0 (SPSS Inc, Chicago, IL) statistical package. Frequencies and descriptive variables were calculated for each group. Categorical variables were compared using a Chi square analysis; continuous variables were compared using the Mann Whitney non parametric independent comparison of medians.

Results

Demographic characteristics of the surgical group and medical group are shown in Table 3. As found in our previous study using the same group of patients,²³ the surgical group had a statistically higher proportion of Hispanic patients but there was no statistical difference in gender, age, or race. Tumors in the surgical group were more often described as leukoplakic, nodular, and/or gelatinous ($p<0.05$) but no statistically significant differences were noted between the groups with respect to area or clinical AJCC stage. Pathology was available for all patients in the surgical group and 27 patients in the interferon group, all of which were consistent with OSSN.

With regards to time implications, the medical group had an average of 2 more actual and imputed number of visits during the course of 1 year compared to the surgical group (Table 3).

When calculating cost using the method of hospital billing (Table 4), there was a statistically significant difference in the total cost for the surgical group versus the medical group ($p<0.005$). Patients undergoing surgery had an average actual \$12,612 increased cost and an average imputed \$12,725 increased cost compared to interferon treatment. There was no statistical difference found for non-interferon medication costs. The cost of office visits was found to be statistically higher in the medical group ($p<0.005$), with the medical group having an average actual \$1,842 increased cost and an average imputed \$1,727 increased cost over the surgical group. This was due to the fact that 4 visits in the surgical group (visits at 1 day, 1 week, 1 month, and 3 months) were bundled in the global period and not billed to the insurer.

When calculating cost using the Medicare allowable method, however, there was no statistically significant difference between total costs in the surgical and medical groups (see Table 4). Interferon was calculated as being an out of pocket cost given Medicare does not

cover the cost of compounded medications. On average, the 48 patients who received drops used approximately 8 bottles of interferon (1 million units per millimeter, 3 million units per millimeter, or both) and incurred a cost of \$1,172 for their drops. For the 9 patients who received injections, they received an average of 5.44 treatments and incurred a cost of \$370 for their injections.

Discussion

In a previous analysis by our group studying the same cohort of patients,²³ and as found by other groups,⁹ patients treated with surgical excision versus interferon had similar treatment outcomes in terms of success and recurrences, suggesting that both treatments are effective in treating OSSN.

When deciding about treatment, financial costs and time considerations may play a larger role in decision making between the physician and the patient and there are several factors to be considered. Overall, we found that the medical group had an average of 2 more actual and imputed number of visits during the course of 1 year. Financially, cost as represented by hospital charges was higher in the surgical group, but cost between the two groups was not statistically different when calculated based on Medicare allowable charges

Financial cost can be identified differently depending on whose perspective is being considered—the patient, the health provider/hospital, or society. Insurance status and coverage plays a large role in determining the out of pocket costs to a patient.

We will first discuss this based on out of pocket costs to the patient. For uninsured patients, hospital billing serves as a close approximation as to what they will be asked to pay out of pocket for procedures and hospital visits. Hospital billing, although often higher than Medicare allowable reimbursements has a precedent for being used to calculate cost in the medical literature.³⁰ Given that hospital billing charges for the surgery group (average cost \$17,598; imputed average cost \$17,944) were significantly higher than the hospital billing charges for the interferon group (average cost \$4,986; imputed average cost \$5,219), medical treatment is the more financially appealing option to uninsured patients.

For insured patients, each insurer may set a different reimbursement for the provider and facility, and patient costs. We chose to also evaluate costs in terms of Medicare allowable reimbursements as they remain the gold standard for setting the fee schedule for many insurance companies and more closely affect the experience of financial cost from the perspective of the insurance company, the patient, and society. Studies in prostate cancer,³¹ lung cancer,³² macular degeneration,³³ retinal detachment repair,³⁴ and macular holes³⁵ have used Medicare allowable reimbursements to establish costs for comparative analysis and cost effectiveness. The out of pocket cost for treatment of OSSN to a Medicare patient would differ based on two factors—whether they had secondary insurance, and if they did, whether the cost of topical medications would be covered. Medicare patients without secondary insurance are responsible for 20% of the Medicare allowable charges, whereas Medicare patients with secondary insurance do not incur out of pocket costs for hospital charges. The only potential cost to a patient with Medicare and secondary insurance would

be the cost of compounded medications like interferon, not typically covered by Medicare but sometimes covered by secondary insurances.

In our analysis of Medicare allowable charges, the expense of interferon (average \$1,172 for topical medication and \$370 for injections in Table 4) was assumed to be an out of pocket expense in the medical group. Thus, for patients insured by Medicare with a secondary insurance that does not cover the cost of interferon, there is a large financial incentive to choose surgical over medical treatment, as there would be no out of pocket cost to the patient for surgery

Financial cost considerations are different if a patient has insurance that covers the cost of compounded medications. In our study, when using the Medicare allowable method and considering hospital costs (incurred by office visits and biopsy costs alone), we assumed the cost of interferon was out of pocket to the patient because Medicare does not cover the cost of compounded medications. However, if the cost of interferon was covered by insurance, the out of pocket cost of medical treatment would actually be lower than surgical treatment. Thus, for a non-Medicare patient or a Medicare patient with a secondary plan which covered interferon, medical treatment would be more financially appealing than surgery.

Similarly, cost considerations would also be different for a Medicare patient who did not have a secondary insurance, as they would be responsible for paying 20% of the Medicare allowable charges.

There is significant variability among insurance plans regarding the financial burden placed on the patient. The actual out of pocket costs to the privately insured patient would be determined by the percentage copay and deductible of their plan and thus may be different than those found in our Medicare allowable analysis. However, given that insurance companies base their charges on some proportion of Medicare allowable charges, the out of pocket cost to the patient of medical treatment would still be lower if the cost of compounded medications was covered. When interferon costs lower, this too would change the pendulum.

Thus, based on out of pocket costs for the patient, an uninsured patient would be most likely to choose interferon (average \$4,986) over surgery (average \$17,598). A patient with Medicare and no secondary insurance would have similar costs with either surgical (20% of the average Medicare allowable charges: \$705.60) or medical treatment (20% of Medicare allowable charges: \$566.20). There was no statistically significant difference between these costs. A patient with Medicare and secondary insurance covering the cost of interferon might choose either therapy given very low or no out of pocket costs with each therapy. A patient with Medicare and a secondary insurance not covering the cost of interferon would most likely choose surgery given the low out of pocket costs for surgery and high interferon costs (\$1,172 average for topical treatment and \$370 average for treatment with injections).

When considering cost from the perspective of providers, hospitals, and society at large, surgical versus medical treatments for OSSN would have different advantages. Hospital billing, as mentioned above, reflects the financial burden that would be incurred by uninsured patients. Our results showed that hospital billing in the surgical group was more

than 2 times higher than medical treatment. Hospital billing charges included charges for the use of the operating room/minor procedure room, microscope, cautery, sutures, irrigating solution, anesthesia, and amniotic membrane if used. Operating room charges varied based on the time spent by the surgeon. As reimbursements for surgical procedures change, this may determine how cost effective surgery is for hospitals and providers.

However, another factor to consider in the cost to providers, hospitals, and society at large is the 2 extra clinic visits found in the medical group. While modest in number, more visits translate to more time spent on the part of the provider, more days missed from a person's job and more time invested in transportation to and from appointments by a patient and his/her caregivers. In the case of many elderly patients, there may be additional costs associated with needing to hire a driver or having a friend or one of their children miss work in order to bring them to their appointments. The nonmedical financial costs of parking, transportation, lodging expenses, caregiver wages, and lost wages from missed work were not considered. In addition, out of pocket costs based on different insurances were not considered. Furthermore, physician time in minutes for surgery and office visits was not tallied; only the number of hospital visits for each patient was calculated. All of these factors would be of interest in future studies. In more recent years, we have lengthened the time period between visits in medically treated patients. Currently, we follow patients every 6–8 weeks for the first 4 months to ensure response to therapy, and then stretch the visits to every 3 months thereafter. With this new protocol we estimate that, on average, a patient would need to be seen 5 times in the first year, which would be more comparable to the surgical group. A future study will better evaluate the cost significance of this protocol change.

To conclude, this study found that interferon treatment involved more time and a higher level of compliance over surgical treatment. Hospital billing charges were higher in the surgical group compared to the interferon group whereas Medicare allowable charges were comparable between the two groups. The out of pocket cost to the patient is dependent on the status and level of insurance coverage. Rather than allowing the bias of different payer mixes effect our comparison between the two treatments, we chose to examine the hospital billing and Medicare allowable charges in order to provide the reader with the true cost of each treatment. Given the clinical equivalency of surgical versus medical treatment, physicians treating patients with OSSN will have to weigh the financial and time costs of each treatment and tailor the treatment accordingly to their patients' circumstances.

As the landscape of financial reimbursement in healthcare evolves and stabilizes, future studies will need to re-evaluate the analysis regarding the cost of each modality in terms of physician work effort, patient out of pocket costs, and the cost to our insurers.

Acknowledgments

Financial Support: Supported by NIH Center Core Grant P30EY014801, Research to Prevent Blindness Unrestricted Grant, Department of Defense (DOD-Grant#W81XWH-09-1-0675). The Ronald and Alicia Lepke Grant, The Lee and Claire Hager Grant, The Jimmy and Gaye Bryan Grant, The Richard Azar Family Grant, The Thornbrough Family Grant. The Gordon Charitable Foundation. (Dr. Karp institutional grants). The Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research and Development's Career Development Award CDA-2-024-10S (Dr. Galor),

References

1. Lee GA, Hirst LW. Ocular surface squamous neoplasia. *Surv Ophthalmol.* 1995; 39(6):429–50. [PubMed: 7660300]
2. Shields JA, Shields CL, De Potter P. Surgical management of conjunctival tumors. The 1994 Lynn B. McMahan Lecture. *Arch Ophthalmol.* 1997; 115(6):808–15. [PubMed: 9194740]
3. Shields, JA.; Shields, CL. *Eyelid, Conjunctival, and Orbital Tumors.* Philadelphia, PA: Lippincott Williams & Wilkins; 2008.
4. Adler E, Turner JR, Stone DU. Ocular surface squamous neoplasia: a survey of changes in the standard of care from 2003 to 2012. *Cornea.* 2013; 32(12):1558–61. [PubMed: 24145630]
5. Shields CL, Kaliki S, Kim HJ, et al. Interferon for ocular surface squamous neoplasia in 81 cases: outcomes based on the American Joint Committee on Cancer classification. *Cornea.* 2013; 32(3): 248–56. [PubMed: 22580436]
6. Kim HJ, Shields CL, Shah SU, et al. Giant ocular surface squamous neoplasia managed with interferon alpha-2b as immunotherapy or immunoreduction. *Ophthalmology.* 2012; 119(5):938–44. [PubMed: 22361315]
7. Shah SU, Kaliki S, Kim HJ, et al. Topical interferon alfa-2b for management of ocular surface squamous neoplasia in 23 cases: outcomes based on American Joint Committee on Cancer classification. *Arch Ophthalmol.* 2012; 130(2):159–64. [PubMed: 22332208]
8. Galor A, Karp CL, Chhabra S, et al. Topical interferon alpha 2b eye-drops for treatment of ocular surface squamous neoplasia: a dose comparison study. *Br J Ophthalmol.* 2010; 94(5):551–4. [PubMed: 19493859]
9. Sturges A, Butt AL, Lai JE, Chodosh J. Topical interferon or surgical excision for the management of primary ocular surface squamous neoplasia. *Ophthalmology.* 2008; 115(8):1297–302. 302 e1. [PubMed: 18294690]
10. Holcombe DJ, Lee GA. Topical interferon alfa-2b for the treatment of recalcitrant ocular surface squamous neoplasia. *Am J Ophthalmol.* 2006; 142(4):568–71. [PubMed: 17011846]
11. Boehm MD, Huang AJ. Treatment of recurrent corneal and conjunctival intraepithelial neoplasia with topical interferon alfa 2b. *Ophthalmology.* 2004; 111(9):1755–61. [PubMed: 15350333]
12. Schechter BA, Rand WJ, Velazquez GE, et al. Treatment of conjunctival papillomata with topical interferon Alfa-2b. *Am J Ophthalmol.* 2002; 134(2):268–70. [PubMed: 12140037]
13. Parrozzani R, Lazzarini D, Alemany-Rubio E, et al. Topical 1% 5-fluorouracil in ocular surface squamous neoplasia: a long-term safety study. *Br J Ophthalmol.* 2011; 95(3):355–9. [PubMed: 20693564]
14. Sepulveda R, Pe'er J, Midena E, et al. Topical chemotherapy for ocular surface squamous neoplasia: current status. *Br J Ophthalmol.* 2010; 94(5):532–5. [PubMed: 19776089]
15. Rudkin AK, Muecke JS. Adjuvant 5-fluorouracil in the treatment of localised ocular surface squamous neoplasia. *Br J Ophthalmol.* 2011; 95(7):947–50. [PubMed: 21252085]
16. Nanji AA, Sayyad FE, Karp CL. Topical chemotherapy for ocular surface squamous neoplasia. *Curr Opin Ophthalmol.* 2013; 24(4):336–42. [PubMed: 23680759]
17. Chen C, Louis D, Dodd T, Muecke J. Mitomycin C as an adjunct in the treatment of localised ocular surface squamous neoplasia. *Br J Ophthalmol.* 2004; 88(1):17–8. [PubMed: 14693762]
18. Rahimi F, Alipour F, Ghazizadeh Hashemi H, et al. Topical mitomycin-C for treatment of partially-excised ocular surface squamous neoplasia. *Arch Iran Med.* 2009; 12(1):55–9. [PubMed: 19111031]
19. Birkholz ES, Goins KM, Sutphin JE, et al. Treatment of ocular surface squamous cell intraepithelial neoplasia with and without mitomycin C. *Cornea.* 2011; 30(1):37–41. [PubMed: 20861726]
20. Kashkouli MB, Heirati A, Pakdel F, et al. Long-term follow-up of invasive ocular surface squamous cell carcinoma treated with excision, cryotherapy, and topical mitomycin C. *Graefes Arch Clin Exp Ophthalmol.* 2012
21. Gupta A, Muecke J. Treatment of ocular surface squamous neoplasia with Mitomycin C. *Br J Ophthalmol.* 2010; 94(5):555–8. [PubMed: 20447963]

22. Khokhar S, Soni A, SinghSethi H, et al. Combined surgery, cryotherapy, and mitomycin-C for recurrent ocular surface squamous neoplasia. *Cornea*. 2002; 21(2):189–91. [PubMed: 11862092]
23. Nanji AA, Moon CS, Galor A, Sein J, Oellers P, Karp CL. Surgical versus Medical Treatment of Ocular Surface Squamous Neoplasia: A Comparison of Recurrences and Complications. *Ophthalmology*. 2014; 121(5):994–1000. [PubMed: 24411578]
24. Centers for Medicare and Medicaid Services. [Accessed October 3, 2013] Physician Fee Schedule. Available at: INTER REF <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/index.html?redirect=/physicianfeesched.html>
25. Centers for Medicare and Medicaid Services. [Accessed October 3, 2013] Florida payment localities by county. 2013. Available at: INTER REF http://medicare.fcsso.com/Fee_resources/138322.asp.html
26. Centers for Medicare and Medicaid Services. [Accessed on March 15, 2014] Development of A Validation Model for RVUs. Available at: INTER REF <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/RVUs-Validation-Modelpdfhtml>
27. Centers for Medicare and Medicaid Services. [Accessed on October 3, 2013] Addendum B - Final OPPS Payment by HCPCS Code for CY. 2013. Available at: INTER REF <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Addendum-A-and-Addendum-B-Updates-Items/January-2013-addendum-B.html>
28. Centers for Medicare and Medicaid Services. [Accessed October 3, 2013] Wage Index Final Rule and Correction Notice Tables. 2013. Available at: INTER REF <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Wage-Index-Files-Items/CMS1252760.html?DLPage=1&DLFilter=2013&DLSort=2&DLSortDir=ascending.html>
29. Centers for Medicare and Medicaid Services. [Accessed October 3, 2013] 2013 Anesthesia conversion factors for Florida-revised. 2013. Available at: INTER REF http://medicare.fcsso.com/Fee_news/246973.asp.html
30. Ciezki JP, Klein EA, Angermeier KW, et al. Cost comparison of radical prostatectomy and transperineal brachytherapy for localized prostate cancer. *Urology*. 2000; 55(1):68–72. [PubMed: 10654897]
31. Corcoran AT, Peele PB, Benoit RM. Cost comparison between watchful waiting with active surveillance and active treatment of clinically localized prostate cancer. *Urology*. 2010; 76(3):703–7. [PubMed: 20381846]
32. Puri V, Crabtree TD, Kymes S, et al. A comparison of surgical intervention and stereotactic body radiation therapy for stage I lung cancer in high-risk patients: a decision analysis. *J Thorac Cardiovasc Surg*. 2012; 143(2):428–36. [PubMed: 22169443]
33. Smiddy WE. Relative cost of a line of vision in age-related macular degeneration. *Ophthalmology*. 2007; 114(5):847–54. [PubMed: 17306878]
34. Chang JS, Smiddy WE. Cost-effectiveness of retinal detachment repair. *Ophthalmology*. 2014; 121(4):946–51. [PubMed: 24411577]
35. Chang JS, Smiddy WE. Cost evaluation of surgical and pharmaceutical options in treatment for vitreomacular adhesions and macular holes. *Ophthalmology*. 2014; 121(9):1720–6. [PubMed: 24835758]

Table 1

Demographic and Clinical Features in Ocular Surface Squamous Neoplasia Treated Surgically versus Medically

	Surgical	Medical	P-value
Number of eyes/patients	49	49	
Age (years), mean [SD]	64 [14]	58 [24]	0.12
Gender, male n [%]	26 [53]	27 [55]	0.84
Race, white n [%]	41 [84]	33 [82.5]	0.33
black n [%]	5 [10]	2 [5]	
other n [%]	3 [6]	5 [12.5]	
Ethnicity, Hispanic n [%]	26 [54]	16 [33]	0.03
Area (mm ²), mean (SD)	24 (30)	34 (36)	0.14
Clinical AJCC stage, n [%]			
T1	13 [27]	5 [10]	0.07
T2	6 [12]	4 [8]	
T3	30 [61]	40 [82]	
Appearance, n [%]			
Leukoplakia	21 [51]	14 [29]	0.03
Papillomatous	9 [18]	10 [22]	0.64
Nodular	28 [57]	15 [31]	0.008
Gelatinous	22 [58]	16 [33]	0.02

n=number of individuals in group SD=standard deviation

Table 2

Medication Costs at the Bascom Palmer Eye Institute in 2013

Antibiotics	\$	ml	Potential duration
Polymyxin B and trimethoprim ophthalmic gtts (generic)	14.5	10	50 days
Dexamethasone, neomycin and polymyxin B gtts (generic)	16	5	25 days
Gentamicin gtt (generic)	8	5	25 days
Moxifloxacin gtts (brand)	104	3	15 days
Gatifloxacin gtts (brand)	90	5	25 days
Ofloxacin gtts (generic)	8	5	25 days
Tobramycin and dexamethasone gtts (brand)	30	2.5	12.5 days
Erythromycin ointment (generic)	22	3.5	21 days
Bacitracin ointment (generic)	64.5	3.5	21 days
Bacitracin zinc and polymixin B sulfate ointment (generic)	11.5	3.5	21 days
Anti-inflammatory agents			
Nepafenac gtts (brand)	132	3	15 days
Ketorolac tromethamine gtts (generic)	15	5	25 days
Fluorometholone 0.1% gtts (generic)	15	5	25 days
Loteprednol etabonate gtts (brand)	127.5	5	25 days
Difluprednate gtts (brand)	126.5	5	25 days
Prednisolone acetate 1% gtts (generic)	10	5	25 days
Cyclosporine 0.05% gtts (brand)	132	30	30 days
Other			
Brimonidine tartrate/timolol maleate (brand)	82.5	5	50 days
Timolol (generic)	8	5	1 mo
Diamox 250mg (generic)	8	7 pills	3 days
Atropine 1% gtts (generic)	17	5	50 days
Acetaminophen and oxycodone (generic)	8	30 pills	7 days
Anti-tumor drugs			
Interferon drops 1 million units/ml	130	3	15 days
Interferon drops 3 million units/ml	180	3	15 days
Interferon injection 3 million units/0.5 ml	68	0.5	1 day

Gtts=drops

Table 3

Time Implications for Ocular Surface Squamous Neoplasia Treated Surgically Versus Medically in the First Year.

Time implications*	Surgical	Medical	P value
# visits to BPEI, actual, mean±SD, (median, range)	5.2±1.6 (5, 2-9)	8.6±4.3 (7, 3-23)	<0.005
# visits to BPEI, imputed [†] mean±SD, (median, range)	6.4±2.0 (6, 2-10)	9.3±4.3 (8, 4-26)	<0.005
Hospital Billing Charges for Clinic Visits (actual) [°]	\$1,3112±507 (\$1,236, \$309-2,472)	\$3,058±1,321 (\$2,572, \$1,336-7,516)	<0.005
Medicare Allowable Charges for Clinic Visits (actual) [‡]	\$547±211 (\$15.5, 128.9-1,031)	\$1,288± 551 (\$1,085.7, \$570.2-\$3,147.8)	<0.005

n=number of patient in each group who incurred a cost in each category; SD=standard deviation; BPEI=Bascom Palmer Eye Institute

* Visits including day of surgery or clinic day that interferon therapy was initiated.

[†] General follow up for surgery: 4 visits between zero to 3 months, and 1 visit between 3 to 6 month, 6 to 9 months, and 9 to 1 year windows. In patients with less than 1 year follow up, visits imputed to fit this general pattern. For example, a patient with 6 months of follow up would have 2 additional visits added. General follow up for medical group, once tumor resolved, follow every 3 months. In patients with less than 1 year follow up, visits imputed to fit this general pattern.

[°] Based upon hospital charges for an office visit based on hospital billing for:

- Level 3 new patient (facility and physician fee): \$409
- Level 3, returning patient (facility and physician fee): \$309

[‡] Based on 2013 Medicare allowable charges for an office visit:

- Level 3 new patient (facility and physician fee): \$183.55
- Level 3, returning patient (facility and physician fee): \$128.88

Table 4
Hospital Billing and Medicare Allowable Charges for Ocular Surface Squamous Neoplasia Treated Surgically versus Medically.

	Hospital billing total charges					Medicare allowable total charges				
	Surg (n)	Surgical Cost	Med (n)	Medical Cost	P value	Surg (n)	Surgical Cost	Med (n)	Medical Cost	P value
Excisional or incisional biopsy costs*	49	\$16,144±7763 (\$13,855) (\$3,169-31,662)	27 22	\$1369 \$0	NA	49	\$2644±1579 (\$1,977) (\$736-5,859)	27 22	\$737 \$0	NA
Pathology cost	49	\$430 ± 0	27 22	\$430 ± 0 \$0	NA NA	49	\$35.59 ± 0	27 22	\$35.59 ± 0 \$0	NA NA
Non-interferon medication cost	48	\$119 ± 316 (\$44.5, \$10-2,205)	24	\$62 ± 49 (\$64.5, \$8-\$192)	0.50	48	\$119 ± 316 (\$44.5, \$10-2,205)	24	\$62 ± 49 (\$64.5, \$8-\$192)	0.50
Interferon medication costs	NA	NA	48 9	\$1172 ± 567 (\$1,125, \$130-2,580) \$370 ± 190 (\$408, \$68-680)	NA	NA	NA	48 9	\$1172 ± 567 (\$1,125, \$130-2,580) \$370 ± 190 (\$408, \$68-680)	NA
Office visit costs [†] (initial & follow up)	49	\$907±458 (\$718, \$409-2,881)	49	\$2,749±1321 (\$2,263, \$1,027-7,207)	<0.005	49	\$730±211 (\$699, \$312-1,215)	49	\$1,159±551 (\$956, \$441-3,019)	<0.005
Actual	49	\$1254±504 (\$1336, \$409-2,881)	49	\$2981±1324 (\$2,572, \$1,336-8,134)	<0.005	49	\$875±261 (\$828, \$312-1,343)	49	\$1257±552 (\$1,086, \$570-3,406)	0.001
Total costs	49	\$17,598±7,624 (\$15,438), (\$2,581-32,845)	49	\$4,986±2,040 (\$4,711) (\$1,567-9,779)	<0.005	49	\$3,528±1610 (\$2,840) (\$1,149-6,939)	49	\$2,831±1,082 (\$2,877) (\$981-5,702)	1.00
Imputed**	49	\$17,944±7,810 (\$15,531) (\$2,581-33,772)	49	\$5,219±1,965 (\$4,874) (\$2,236-10,706)	<0.005	49	\$3,672±1,656 (\$3,014) (\$1,149-6,939)	49	\$2,928±1,033 (\$2,901) (\$1,470-5,702)	0.42

Patients with ocular surface squamous neoplasia may be treated surgically or medically. Medical treatment will most likely involve more time whereas surgical treatment can be more costly or similar depending on insurance coverage.