

# Prophylactic Leukotriene Inhibitor Therapy for the Reduction of Capsular Contracture in Primary Silicone Breast Augmentation: Experience with over 1100 Cases

Stephen D. Bresnick, M.D.

Encino, Calif.



**Background:** The role of leukotriene inhibitors used immediately postoperatively to potentially influence the development of capsular contracture is unknown. The purpose of this study was to evaluate the incidence of capsular contracture among women undergoing primary smooth silicone gel breast augmentation, with or without postoperative leukotriene inhibitor therapy.

**Methods:** Between 2007 and 2013, 1122 consecutive women undergoing primary silicone gel breast augmentation were evaluated retrospectively. All underwent augmentation with smooth, Mentor Memory Gel implants, using a dual-plane technique, with periareolar or inframammary approaches. Patients were treated voluntarily with either no leukotriene inhibitor, montelukast (Singulair), or zafirlukast (Accolate) for 3 months. All patients received informed consent for the off-label use of leukotriene inhibitors. Liver function studies were obtained for all patients undergoing Accolate therapy after 1 month of therapy. The presence of capsular contracture was measured by the Baker scale at 1 year postoperatively.

**Results:** Patients receiving Accolate therapy ( $n = 520$ ) demonstrated an encapsulation rate of 2.19 percent. Women receiving Singulair therapy ( $n = 247$ ) had an encapsulation rate of 3.27 percent. Patients not receiving leukotriene inhibitor therapy had an encapsulation rate of 5.02 percent. There were no long-term complications among patients evaluated.

**Conclusions:** Accolate therapy used for 3 months postoperatively was associated with significantly lower capsular contracture rates compared with untreated patients at 1-year follow-up ( $p < 0.05$ ). Patients treated with Singulair demonstrated lower contracture rates compared with controls, but the differences were not statistically significant. The findings suggest that Accolate therapy, with monitoring and consent, reduces the incidence of capsular contracture following primary smooth silicone gel breast augmentation. (*Plast. Reconstr. Surg.* 139: 379e, 2017.)

**CLINICAL QUESTION/LEVEL OF EVIDENCE:** Therapeutic, III.

From private practice.

Received for publication February 1, 2016; accepted July 14, 2016.

Presented at the 63rd Annual Meeting of the California Society of Plastic Surgeons, in San Francisco, California, May 24 through 27, 2013; and the American Society for Aesthetic Plastic Surgery Annual Meeting, in San Francisco, California, April 24 through 29, 2014.

Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Society of Plastic Surgeons. All rights reserved. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/PRS.0000000000003006

Capsular contracture remains the most common complication of aesthetic breast augmentation despite advances in the understanding of the biological processes that appear to be involved. The role of biofilms in the pathogenesis of capsular contracture has been reported extensively; they are believed to play an important role.<sup>1,2</sup> Recent advances in antibiotic irrigation<sup>3,4</sup> and the use of skin barriers and nipple shields<sup>5,6</sup> has assisted in the reduction of capsular contracture. Form-stable implant studies with textured devices have also

**Disclosure:** The author has no financial interest in any of the products, devices, or drugs mentioned in this article.

shown lower capsular contracture rates compared with smooth round devices. Nevertheless, despite these advances, a significant number of women develop capsular contracture following breast augmentation and require revision surgery or live with discomfort, deformity, or suboptimal results.

The use of leukotriene inhibitors for the treatment of capsular contracture was reported as early as 2002,<sup>7,8</sup> and multiple studies have shown benefits in softening breasts and reducing the severity of capsular contracture with either montelukast (Singulair; Merck, Kenilworth, N.J.) or zafirlukast (Accolate; AstraZeneca Pharmaceuticals, Wilmington, Del.).<sup>9–13</sup> However, the effects of using these medications immediately postoperatively, before any evidence of capsular contracture may be present, is unknown. Currently, there is no clear standard of care for the use of these off-label medications, and little information is available about which medication may be more or less beneficial.

A high-volume aesthetic breast practice with a single surgeon performing a standardized procedure provided an excellent opportunity to evaluate the effects of leukotriene inhibitor therapy. The author timely implemented the advances advocated by research in our specialty with regard to reduction of biofilm exposure, using triple-antibiotic/povidone-iodine irrigation and the use of skin barriers/nipple shields. Despite these techniques, which lowered the encapsulation rates among our patients to well below national averages reported,<sup>14</sup> we desired to explore the potential benefits of leukotriene therapy used prophylactically in the early postoperative period.

## PATIENTS AND METHODS

The study was performed with a retrospective review of 1122 consecutive women undergoing primary, silicone gel breast augmentation. Over time, the author added leukotriene inhibitor therapy to the postoperative treatment of patients. The first group of patients were treated without leukotriene therapy (2007 to 2009). Consecutive patients agreeing to the off-label use of leukotriene inhibitors were then studied. The second group of consecutive patients were offered Singulair therapy (2009 to 2010) postoperatively, whereas all other aspects of the surgical technique and care remained the same. The author then offered Accolate therapy (2010 to 2012) to the final group of patients undergoing breast augmentation.

All patients were between the ages of 22 and 60 years and gave informed consent for the use of silicone gel breast implants. All patients were

provided with informed consent for the use of Mentor Memory Gel silicone implants (Mentor Worldwide, Irvine, Calif.) and the off-label use of triple-antibiotic irrigation containing povidone-iodine (Betadine; Purdue Frederick Co., Norwalk, Conn.). In addition, a detailed informed consent was provided for the off-label use of either Singulair or Accolate. All patients were adequately informed of the risks, potential unknown benefits, cost, and potential side effects of leukotriene therapy with both verbal and written consent. Patients were informed that taking leukotriene inhibitor medications was voluntary and that they could discontinue these medications at any time for any reason. In particular, patients were counseled on the potential significant risks of leukotriene inhibitors, including the uncommon risk of chemical hepatitis, liver failure, and even death, all of which were reported in Accolate U.S. Food and Drug Administration postapproval studies for the treatment of asthma.

Patients chose augmentation with either a periareolar or inframammary approach. Silicone breast augmentation procedures were performed by the author, using a standardized, dual-plane technique. All patients were treated with preoperative intravenous antibiotics, either a 1-g dose of cephazolin or 600 mg of clindamycin, selected based on allergy profiles. Before insertion of implants, triple-antibiotic irrigation [50,000 U of bacitracin, 1 g of Ancef (GlaxoSmithKline, Middlesex, United Kingdom), and 80 mg of gentamicin] with the addition of 50 ml of povidone-iodine in 500 ml of normal saline was used. All implants were placed with powder-free glove changes and inserted through a skin barrier/nipple shield using Tegaderm (3M, St. Paul, Minn.) dressings. A standardized breast implant massage program was initiated on postoperative day 2.

Patients treated with leukotriene inhibitors began medication the day after surgery. Patients with a history of hepatitis or liver disease were excluded. Patients were treated with the standard dosing for each medication, recommended by the manufacturer for on-label use. Singulair 10 mg/day or Accolate 20 mg twice daily was used. Patient compliance with the recommended dosage was encouraged. Patients were asked to report perceived side effects of the medications, and medications were discontinued at any time the patient felt that the side effects were significant.

All patients receiving Accolate therapy underwent liver function studies 4 weeks after the initiation of Accolate therapy. Elevation of transaminases resulted in discontinuation of the

medication. Follow-up liver function studies were performed at 2-week intervals, until transaminases normalized. Patients who demonstrated Baker grade III or IV capsular contractures at 3-month follow-up were offered 3 additional months of either Singulair or Accolate therapy. Liver function studies were repeated after 3 months of Accolate therapy for patients choosing to continue Accolate for a 6-month course.

All patients were evaluated at frequent follow-up appointments by both the author and a plastic surgery nurse specialist, including early postoperative visits, 1 month, 3 months, 6 months, and 1 year postoperatively. Capsular contracture was evaluated by the Baker scale. Patients with grade III or IV capsular contractures were considered clinically encapsulated. Statistical comparison of the groups was performed with the Barnard exact test.<sup>15</sup>

### RESULTS

Table 1 shows the groups of consecutive patients who completed the study protocol with 1-year follow-up. A high degree of compliance with the study was achieved, with 84.8 percent of Accolate-treated patients, 82.2 percent of Singulair-treated patients, and 79.4 percent of no leukotriene inhibitor-treated patients completing the 1-year follow-up. Of the patients evaluated, 72 percent underwent a periareolar approach and 28 percent chose an inframammary incision. There were no differences in the percentage of patients choosing a particular incision type between the groups. For patients offered leukotriene therapy following breast augmentation, 22 patients declined to participate and were not included in the study. For patients treated with Singulair, 2.5 percent of patients claimed to discontinue the medication because of side effects or cost. The percentage of patients discontinuing Accolate was 6.2 percent for minor side effects or cost. Three of 520 patients treated with Accolate therapy (0.58 percent) demonstrated mild elevation of transaminases and discontinued the medication. Transaminases returned to normal within 2 weeks after discontinuing the medication for two patients and within 4 weeks for one patient. A summary of the most common side effects reported by patients for each leukotriene inhibitor is listed in Table 2.

The rate of capsular contracture for patients undergoing primary silicone gel breast augmentation with or without leukotriene inhibitor therapy is listed in Table 3. Women undergoing breast augmentation followed by 3 months of Accolate therapy demonstrated capsular contracture rates

**Table 1. Numbers of Patients Undergoing Primary Silicone Gel Breast Augmentation Treated with or without Leukotriene Inhibitors**

Therapy	No. (%)
No leukotriene inhibitors	355 (31.6)
Singulair	247 (22.0)
Accolate	520 (46.3)

**Table 2. Common Side Effects Reported by Patients Taking Leukotriene Inhibitor Medications after Primary Silicone Gel Breast Augmentation**

Therapy	Side Effects
Singulair	Headache, GI symptoms, fatigue, rash
Accolate	Vivid dreams, insomnia, headache, mood changes, rash, muscle pain, GI symptoms

GI, gastrointestinal.

**Table 3. Percentage of Patients Demonstrating Capsular Contracture at 1 Year after Primary Silicone Gel Breast Augmentation**

Therapy	% of Patients with Capsular Contracture	95% CI (Jeffreys)
No leukotriene inhibitor	5.02	0.0284–0.0819
Singulair	3.27	0.0126–0.0701
Accolate	2.19*	0.0101–0.0398

\* $p < 0.05$ .

significantly lower compared with women not treated with leukotriene inhibitors postoperatively ( $p < 0.05$ ). Patients treated with Singulair therapy showed capsular contracture rates lower than patients not treated with leukotriene inhibitors, but the differences were not statistically significant. For patients treated with Singulair for 3 months, two patients developed grade III/IV capsular contractures that improved (to grade II) with an additional 3 months of therapy. For patients treated with Accolate for 3 months, five patients demonstrating grade III or IV capsular contractures at 3 months postoperatively improved with an additional 3 months of therapy (to grade II).

Table 4 demonstrates the distribution of capsular contractures based on incision location for each of the groups studied. All groups of patients demonstrated a greater percentage of capsular contractures with the periareolar incision compared with the inframammary incision. For patients treated with Accolate, the capsular contracture rates were similar comparing both incision locations. However, there were no statistically significant differences between the groups

**Table 4. Number and Percentage of Patients Demonstrating Capsular Contracture by Incision Location at 1 Year after Silicone Gel Breast Augmentation**

Therapy	Periareolar (%)	Inframammary (%)	Total (%)
No leukotriene inhibitor	11/189 (5.82)	2/70 (2.86)	13/259 (5.02)
Singulair	4/105 (3.81)	1/48 (2.08)	5/153 (3.27)
Accolate	6/260 (2.31)	2/115 (1.74)	8/375 (2.19)

based on incision location. Confidence intervals for each of the groups shown in Tables 3 and 4 were calculated using Jeffreys confidence interval analysis.<sup>16</sup>

## DISCUSSION

The results of this study demonstrate that Accolate used for 3 months postoperatively after primary silicone gel breast augmentation with smooth surface gel implants is associated with significantly lower capsular contracture rates at 1-year follow-up compared with patients not treated with a leukotriene inhibitor postoperatively. This is the first report that demonstrates that prophylactic leukotriene inhibitor therapy used for patients undergoing primary silicone gel breast augmentation is correlated to a lower capsular contracture rate at 1-year follow-up.

Recently, Graf et al.<sup>17</sup> reported reduction in capsular contracture following the prophylactic use of Singulair in patients undergoing textured silicone breast augmentation procedures including primary augmentation, augmentation mastopexy, and augmentation revision. The study involved a small group of patients, 84 total, in which 37 were treated with Singulair. Two surgeons performed the procedures, with one surgeon's patients receiving Singulair and the other surgeon's patients not receiving a leukotriene receptor antagonist. They reported a reduced severity of capsular contracture in patients treated with Singulair. However, the study of Graf et al. reports a small group of patients undergoing multiple types of operations including revisions. Several different access incisions were used with variations in surgical pocket location and two different surgeons, only one of whom treated patients with Singulair. In the present study, with a much larger sample size, and a greater degree of uniformity, we did note a lower capsular contracture rate compared with untreated patients, but the difference was not statistically significant. The difference in findings may have been related to

the fact that different implant surfaces were used comparing the two studies, all the patients in the present study were primary augmentation procedures, and the current study is a single-surgeon series compared with the two-surgeon series of Graf et al.

In the current study, Singulair was found to be helpful in capsular contracture reduction, but the differences were less impressive than with Accolate and not statistically significant. Because both medications are known to be leukotriene inhibitors, why would one drug be more useful than the other?

The clinical pharmacology and recent research studies suggest possible explanations for these findings. Three cysteinyl leukotrienes, leukotriene C<sub>4</sub>, leukotriene D<sub>4</sub>, and leukotriene E<sub>4</sub>, are products of arachidonic acid metabolism and are released from cells associated with the inflammatory response. These compounds bind to cysteinyl leukotriene receptors that are found on smooth muscle cells and inflammatory cells. When leukotrienes bind to the cysteinyl leukotriene receptor, multiple effects, including cellular contraction, edema, and altered cellular activity associated with inflammation, may occur. Montelukast (Singulair) inhibits the actions of one leukotriene, leukotriene D<sub>4</sub>, at the cysteinyl leukotriene receptor.<sup>18</sup>

Zafirlukast (Accolate) is a competitive receptor antagonist for leukotrienes, and is known to antagonize the contractile activity of three different leukotrienes, including leukotriene C<sub>4</sub>, leukotriene D<sub>4</sub>, and leukotriene E<sub>4</sub>. These leukotrienes are associated with the inflammatory process, smooth muscle contraction, and cellular contraction.<sup>19</sup> Zafirlukast (Accolate) competitively inhibits three different leukotrienes, rather than the one leukotriene inhibited by Montelukast (Singulair). Although there is no evidence that Accolate is more potent in asthma treatment than Singulair, it may be that it may offer a more robust effect on inhibiting the encapsulation process. Furthermore, the leukotrienes that Singulair does not inhibit, leukotriene C<sub>4</sub> and leukotriene E<sub>4</sub>, may be important in the pathogenesis of capsular contracture. Further studies will be necessary to characterize the differences between these medications on capsular contracture.

Studies have supported the biomolecular basis for capsular contracture involving leukotriene receptors.<sup>20,21</sup> Investigators have shown significantly increased levels of leukotriene receptor activity in patients undergoing capsulectomy for severe capsular contracture compared with

controls without encapsulation. These findings support a possible role for antileukotriene drugs, which may interfere with the activation of leukotriene receptors.

Numerous investigators have demonstrated the benefit of leukotriene inhibitors in the treatment of small numbers of patients with capsular contracture.<sup>8,9,11,12</sup> Huang and Handel reported benefit with the use of Singulair in a group of 19 patients seen with capsular contracture.<sup>10</sup> The authors noted that more than half of the patients improved with Singulair therapy, with a reduction or resolution of capsular contracture. Several patients treated prophylactically with Singulair did not have recurrence. The effect of Accolate on early capsular contracture on primary saline breast augmentation was evaluated in 37 patients demonstrating early capsular contracture.<sup>11</sup> Patients were treated for up to 6 months with Accolate therapy and liver function studies were followed. The results demonstrated that 75 percent of patients had improvement or resolution of early capsular contracture with a mean follow-up of 6.3 months. These studies and others have demonstrated the benefits of leukotriene inhibitors in the treatment of early capsular contracture.

Little is known about the effects of leukotriene inhibitors on the formation and pathogenesis of capsular contracture when used prophylactically. As the inflammatory reaction to trauma, bacteria, blood products, and/or inflammatory mediators progresses, it is believed that myofibroblasts and macrophages form in the immature implant capsule.<sup>22</sup> These cells are known to possess receptors for many inflammatory mediators, including a rich population of cysteinyl leukotriene receptors. It is at this early stage when leukotriene inhibitors may block the receptor and interfere with contractile and inflammatory processes associated with clinical capsular contracture. This hypothesis supports the findings of this study and also suggests why clinicians have reported more success with leukotriene inhibitor therapy when used early in capsular contracture cases.

The studies of capsular contracture and leukotriene inhibitors in the plastic surgery literature have not, as of this time, documented mortality or serious morbidity from the use of leukotriene inhibitors, including Accolate therapy. Many plastic surgeons currently use leukotriene inhibitors to some extent in their practices for the treatment of capsular contracture, but the prevalence, side effects, and benefit of this treatment have not been reported in depth by plastic surgeons. Outside of our specialty, there are more data regarding

Accolate and the risks associated with its use. There is variability in the reports of safety using Accolate as an on-label medication. Although postmarketing data reported by Gryskiewicz<sup>23</sup> demonstrated morbidity and mortality in a small number of asthma patients treated with Accolate, an English landmark study of approximately 8000 patients demonstrated that Accolate was a well-tolerated drug for the treatment of asthma, with few associated adverse effects.<sup>24</sup>

All medications prescribed by physicians for the management of medical conditions carry with them risk of adverse side effects. The statin drugs, although usually well tolerated and extensively prescribed, may cause elevation of transaminases, rhabdomyolysis, increased risk of new-onset diabetes in postmenopausal women, and rarely death from liver failure. However, the potential benefits of this class of medication is felt by patients and physicians to outweigh the risks, and therefore statins are used extensively.

It is difficult to compare our patients with capsular contracture risk to patients at risk for cardiovascular disease. For our patients, the concern is about quality of life. Our capsular contracture patients are not suffering a life-threatening disease. However, this condition subjects patients to pain, deformity, asymmetry, and significant costs associated with treatment. Many patients live with severe capsular contracture for many years. This does affect quality of life. It is certainly reasonable to discuss the potential benefits and risks of leukotriene inhibitor therapy with patients and the options for off-label use of this class of medications. It is important to review in detail the risk of serious liver injury, as rare as it may be. Furthermore, the author believes that a detailed written informed consent discussing the off-label, voluntary use of leukotriene inhibitor medications, including their associated risks, should be a prerequisite for offering these medications to patients.

The hesitation of some plastic surgeons to treat patients with leukotriene inhibitors may relate to a lack of information regarding the efficacy of treatment and concerns regarding patient safety. Other than a few studies published in the past 10 years with small groups of patients, little is known about options, outcomes, and risks of leukotriene inhibitor therapy when used for the treatment of capsular contracture. In 2003, an investigation by our Society was published that reviewed U.S. Food and Drug Administration data from postmarketing reports.<sup>23</sup> In this report, in the majority of patients, elevated liver enzyme

levels returned to normal or nearly normal after Accolate therapy was stopped. In extremely rare cases, patients developed hepatitis and/or hepatic failure and required liver transplantation. The majority of these patients had multiple medical problems and were on multiple medications. The reports of patient morbidity or mortality were not scientifically or otherwise verified as to a cause-and-effect relationship associated with Accolate therapy, but the medication was felt to play a role in the pathogenesis of hepatotoxicity in a small number of patients. It was not clear whether periodic serum transaminase testing would have improved outcome among those demonstrating hepatotoxicity or reduced morbidity and mortality. In this study, three of 520 patients (0.58 percent) treated with Accolate showed elevated transaminases at 30 days of treatment, with complete normalization of transaminases after discontinuation of the medication and retesting. There were no known long-term complications or injuries associated with the use of leukotriene inhibitors.

The results of this study suggest that Accolate can be given prophylactically in a safe and effective manner. However, we are not advocating the routine prophylactic treatment of all postoperative, smooth silicone breast augmentation patients with Accolate. We believe that the plastic surgeon in consultation with the patient should decide with the patient whether this prophylactic treatment would be beneficial or desired. For patients very concerned with minimizing capsular contracture and who wish for or are preferred candidates for smooth implants, Accolate therapy may make sense. Patients should be counseled preoperatively about the potential benefits and risks of therapy and the need to monitor transaminase levels if therapy is to be undertaken.

A particular subgroup of patients may benefit from Accolate therapy. Because studies suggest that periareolar incisions are associated with a higher incidence of capsular contracture,<sup>25,26</sup> patients who undergo this incision may in particular benefit from prophylactic therapy and can be counseled in this regard. This is also supported by data in the current study (Table 4), where patients undergoing periareolar augmentation without a leukotriene inhibitor had a capsular contracture rate of 5.82 percent, whereas patients having a periareolar augmentation with postoperative Accolate had a capsular contracture rate of 2.31 percent.

The findings of this study also have implications for other potentially beneficial uses of Accolate therapy for patients not treated with prophylactic leukotriene inhibitors. For most

patients, capsular contracture begins with tightening of the breast pocket with limitations of implant movement and breast softness. This often begins early in the postoperative period. Skilled breast surgeons can assess patients early postoperatively and predict who may be at the most risk for capsular contracture. Patients with limited implant mobility, reduced pocket dimensions on implant displacement, and reduced implant compliance may benefit from Accolate therapy before a diagnosed capsular contracture begins. We are currently interested in the potential use of Accolate in managing these patients.

The current study demonstrates that Accolate therapy reduced capsular contracture formation when used in the first 3 months after breast augmentation with smooth surface silicone gel implants. Patients treated with Singular had lower capsular contracture rates than patients not treated with a leukotriene inhibitor, but the differences were not statistically significant. The addition of Accolate reduced the encapsulation risk by over 50 percent. The medication was tolerated well by almost 95 percent of patients, with no irreversible side effects noted in the study. Further study of the safety and efficacy of leukotriene inhibitors in the prevention and/or early treatment of capsular contracture is encouraged.

*Stephen D. Bresnick, M.D.*

16633 Ventura Boulevard, Suite 110  
Encino, Calif. 91436  
drbresnick@yahoo.com

## REFERENCES

1. Wixtrom RN, Stutman RL, Burke RM, Mahoney AK, Codner MA. Risk of breast implant bacterial contamination from endogenous breast flora, prevention with nipple shields, and implications for biofilm formation. *Aesthet Surg J*. 2012;32:956–963.
2. Tamboto H, Vickery K, Deva AK. Subclinical (biofilm) infection causes capsular contracture in a porcine model following augmentation mammoplasty. *Plast Reconstr Surg*. 2010;126:835–842.
3. Adams WP Jr, Conner WC, Barton FE Jr, Rohrich RJ. Optimizing breast-pocket irrigation: The post-Betadine era. *Plast Reconstr Surg*. 2001;107:1596–1601.
4. Adams WP Jr, Rios JL, Smith SJ. Enhancing patient outcomes in aesthetic and reconstructive breast surgery using triple antibiotic breast irrigation: Six-year prospective clinical study. *Plast Reconstr Surg*. 2006;117:30–36.
5. Collis N, Mirza S, Stanley PR, Campbell L, Sharpe DT. Reduction of potential contamination of breast implants by the use of 'nipple shields'. *Br J Plast Surg*. 1999;52:445–447.
6. Giordano S, Salmil A. Nipple shields as an additional tool to pocket irrigation in reducing capsular contracture after cosmetic breast augmentation. *Plast Reconstr Surg*. 2014;134(Suppl):386.

7. Schlesinger SL, Ellenbogen R, Desvigne MN, Svehlak S, Heck R. Zafirlukast (Accolate): A new treatment for capsular contracture. *Aesthet Surg J*. 2002;22:329–336.
8. Schlesinger SL, Desvigne MN, Ellenbogen R, Svehlak S, Heck R. Results of using zafirlukast (Accolate) and montelukast (Singulair) for treatment of capsular contracture. *Aesthet Surg J*. 2003;23:101–102.
9. Scuderi N, Mazzocchi M, Fioramonti P, Bistoni G. The effects of zafirlukast on capsular contracture: Preliminary report. *Aesthetic Plast Surg*. 2006;30:513–520.
10. Huang CK, Handel N. Effects of Singulair (montelukast) treatment for capsular contracture. *Aesthet Surg J*. 2010;30:404–408.
11. Reid RR, Greve SD, Casas LA. The effect of zafirlukast (Accolate) on early capsular contracture in the primary augmentation patient: A pilot study. *Aesthet Surg J*. 2005;25:26–30.
12. Mazzocchi M, Dessy LA, Alfano C, Scuderi N. Effects of zafirlukast on capsular contracture: Long-term results. *Int J Immunopathol Pharmacol*. 2012;25:935–944.
13. Scuderi N, Mazzocchi M, Rubino C. Effects of zafirlukast on capsular contracture: Controlled study measuring the mammary compliance. *Int J Immunopathol Pharmacol*. 2007;20:577–584.
14. Cunningham B, McCue J. Safety and effectiveness of Mentor's MemoryGel implants at 6 years. *Aesthetic Plast Surg*. 2009;33:440–444.
15. Barnard GA. Significance tests for 2 X 2 tables. *Biometrika* 1947;34:123–138.
16. Brown LD, Cui TT, DasGupta A. Interval estimation for a binomial proportion. *Stat Sci*. 2001;16:101–133.
17. Graf R, Ascenço AS, Freitas Rda S, et al. Prevention of capsular contracture using leukotriene antagonists. *Plast Reconstr Surg*. 2015;136:592e–596e.
18. U.S. Food and Drug Administration. Updated information on leukotriene inhibitors: Montelukast (marketed as Singulair) 2009. Available at: <http://www.drugs.com/pro/singulair.html>. Accessed February 15, 2016.
19. U.S. Food and Drug Administration. Updated information on leukotriene inhibitors: Zafirlukast (marketed as Accolate) 2009. Available at: <http://www.drugs.com/pro/accolate.html>. Accessed February 17, 2016.
20. Grella E, Grella R, Siniscalco D, et al. Modification of cysteinyl leukotriene receptor expression in capsular contracture: Preliminary results. *Ann Plast Surg*. 2007;58:212–214.
21. Grella E, Grella R, Siniscalco D, et al. Modification of cysteinyl leukotriene receptors expression in capsular contracture: Follow-up study and definitive results. *Ann Plast Surg*. 2009;63:206–208.
22. Hwang K, Sim HB, Huan F, Kim DJ. Myofibroblasts and capsular tissue tension in breast capsular contracture. *Aesthetic Plast Surg*. 2010;34:716–721.
23. Gryskiewicz JM. Investigation of Accolate and Singulair for treatment of capsular contracture yields safety concerns. *Aesthet Surg J*. 2003;23:98–101.
24. Twaites BR, Wilton LV, Shakir SA. Safety of zafirlukast: Results of a postmarketing surveillance study on 7976 patients in England. *Drug Saf*. 2007;30:419–429.
25. Stevens WG, Nahabedian MY, Calobrace MB, et al. Risk factor analysis for capsular contracture: A 5-year Sientra study analysis using round, smooth, and textured implants for breast augmentation. *Plast Reconstr Surg*. 2013;132:1115–1123.
26. Wiener TC. Relationship of incision choice to capsular contracture. *Aesthetic Plast Surg*. 2008;32:303–306.