## SYSTEMATIC REVIEW



# Analyzing the Efficacy of Isotretinoin in Treating Dissecting Cellulitis: A Literature Review and Meta-Analysis

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#### Abstract

**Background and Objective** Dissecting cellulitis of the scalp is a primary scarring alopecia. Isotretinoin is commonly referenced in the literature as a treatment for dissecting cellulitis. The objective of this article was to conduct a review and meta-analysis to assess the efficacy of isotretinoin for treating dissecting cellulitis of the scalp.

**Methods** The following databases were searched for articles prior to 23 June, 2019: PubMed, Embase, Cochrane Central, CINAHL, and Web of Science. Multi-patient studies (more than three) that reported on the administration of isotretinoin for dissecting cellulitis were included. A pooled meta-analysis for improvement of disease burden after isotretinoin administration in patients with dissecting cellulitis of the scalp was performed. A fixed-effects model was used.

**Results** Five articles were ultimately used for the quantitative meta-analysis. The overall efficacy rate of isotretinoin in treating dissecting cellulitis of the scalp was estimated to be 0.9 with a 95% confidence interval (0.81–0.97). The sensitivity analysis suggested that the overall efficacy is still very high, with a range of 0.83–0.94. Recurrence was seen in 24% (6/25) of patients. Common associated diseases amongst patients with dissecting cellulitis of the scalp were acne conglobata 20% (30/151) and hidradenitis suppurativa 19% (11/72).

**Conclusions** Isotretinoin is an effective treatment for improving symptoms of dissecting cellulitis of the scalp. Disease recurrence is a common finding for those who undergo successful treatment.

# **Key Points**

This review and meta-analysis found isotretinoin to be an effective treatment for improving symptoms of dissecting cellulitis.

Recurrence after treatment was cited in a minority of patients treated with isotretinoin.

Tumor necrosis factor- $\alpha$  inhibitors, adalimumab and infliximab, as well as ALA-PDT treatment have been detailed in case studies as potentially effective off-label treatments for refractory dissecting cellulitis.

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## 1 Introduction

Dissecting cellulitis of the scalp (DCS), or perifolliculitis capitis abscedens et suffodiens, is a rare, primary neutrophilic scarring alopecia [1]. Dissecting cellulitis of the scalp

belongs to the "follicular occlusion tetrad," composed of hidradenitis suppurativa, acne conglobate, and pilonidal cysts [2]. Dissecting cellulitis of the scalp is characterized by multiple confluent, suppurative nodules on the scalp that can cause patchy hair loss [3]. The nodules are often associated with pain and pruritus [4, 5]. Inflammatory nodules and abscesses may combine and with prolonged disease may lead to scarring alopecia [6]. The disease can be physically disfiguring and emotionally traumatic owing to the cosmetic appearance of the scalp and difficulty sleeping because of pressure placed on the nodules [3]. The disease has historically been cited as occurring predominantly in young men (aged 18–40 years) of African descent [7], but has recently been shown to occur in other skin phototypes as well [2, 5, 8, 9].

Common treatments for dissecting cellulitis are oral antibiotics (doxycycline, azithromycin, rifampicin), isotretinoin, intralesional triamcinolone acetate, and surgical excision or drainage [4, 10]. Oral antibiotics are often first-line treatment for mild DCS [9]. Isotretinoin is a commonly used treatment for severe DCS, or DCS that is recalcitrant to other therapies such as oral and topical antibiotics [11–14]. Historically, documented use of isotretinoin for treating DCS has been largely limited to case reports consisting of one or two patients [11–14]. In the past 5 years, there have been many more multi-patient studies conducted that have used isotretinoin to treat dissecting cellulitis [4, 5, 8, 9, 15]. This literature review analyzes these studies to attempt to determine whether isotretinoin is effective in decreasing the severity of dissecting cellulitis.

## 2 Methods

## 2.1 Search Strategies

The following databases were searched for articles prior to 23 June, 2019: PubMed, Embase, Cochrane Central, CINAHL, and Web of Science. Search terms included "Accutane AND dissecting cellulitis", "Isotretinoin AND dissecting cellulitis," "Isotretinoin AND perifolliculitis capitis abscedens et suffodiens", and "Isotretinoin AND primary cicatricial alopecia". All applicable studies were exported from their respective databases into Endnote for subsequent de-duplication, abstract review, and full-text review. Studies that were ultimately included met criteria for primary articles that detailed the use of isotretinoin to treat dissecting cellulitis. Articles of any age were included.

## 2.2 Inclusion and Exclusion Criteria

The initial number of articles (six databases) was 369. The number of articles after de-duplication was 164. Inclusion

criteria were articles written in English, involve the use of isotretinoin, use in human subjects, and details a dermatologic condition. Exclusion criteria were not a multi-patient study (more than three patients), not a primary research article (e.g., review article, abstract only), does not administer isotretinoin (discussion only), and does not discuss isotretinoin AND dissecting cellulitis.

## 2.3 Outcome Measure

The primary outcome measure for this meta-analysis was successful improvement of disease after isotretinoin treatment. The definition for treatment success varied among studies, with some studies citing complete resolution of disease while others citing only improvement in disease burden. Therefore, "improvement of disease" was used to standardize the outcome measure across studies. Eligible outcomes included decrease in number of nodules, decrease in inflammation, regrowth of hair, and partial or complete remission of disease. Recurrence was defined as any return of inflammation or nodules after discontinuing isotretinoin.

## 2.4 Data Extraction

The following study characteristics were collected in Excel: first author; year of publication; study design; years of study; number of patients treated overall; number of patients treated with isotretinoin; location of treatment center; age of patients (mean and range); skin type of patient population; male/female ratio; interventions used (past and present); treatment instructions; dose administered; treatment length; cumulative dosing; follow-up interval; success (%); recurrence (%); family history; associated comorbidities; associated pruritis; associated pain; number of nodules (between one and five); number of nodules (greater than five); bacterial culture results. All study data were compiled and displayed in Table 1. Study authors were contacted about any potential discrepancies in data.

## 2.5 Data Analysis and Statistical Methods

Overall efficacy of isotretinoin in treating DCS was estimated through a meta-analysis using R package "metafor" from R 3.5.2 [16]. For the purposes of the statistical analysis, efficacy was defined as "any improvement in dissecting cellulitis after use of isotretinoin".

Cochran's *Q* test was used to test heterogeneity among studies. As there was no evidence of heterogeneity, a fixed-effect model was used. Freeman–Tukey (double arcsine) transformation for proportions was used [17]. Sensitivity analysis was performed by estimating the pooled efficacy after excluding one study at a time. Fixed-effect models were also used. Ninety-five percent confidence intervals (CIs)

Table 1 Study characteristics [4, 5, 8, 9, 15]

	Lee [9]	Segurado-Miravalles [5]	Badaoui [4]	Qi [8]	Tan [15]
Study design	Retrospective	Retrospective	Retrospective	Retrospective	Refrospective
Years	1995–2015	N/A	1996–2013	2007–2013	1997–2001
Total no. of patients treated	99	21	51	59	6 patients with dissecting cellulitis, 112 patients overall
No. of patients treated with isotretinoin	16	∞	35	6	4
Location	Taiwan	Spain	France	China	Canada
Age (mean, range in years)	24.9, 12–59	32.8, 18–58	26.6, 15–62	27.4, 12–42	N/A, 25–42
Skin phototype		18/21 were Caucasian	65% had skin phototypes IV-VI	Chinese patients, Asian skin types	3 Caucasian, 1 Indian, 2 African American, 4 among these were given isotretinoin
Male/female ratio	63/3	17/4	50/1	8/1	0/9
Scalp location	Vertex (89.4%), or (59/66)	Vertex (71.4%) or (15/21)	Vertex (49%) or (25/51)	N/A	N/A
Interventions	Isotretinoin, possible combined use with prednisolone, prior use of antibiotics	Isotretinoin, additional prior antimicrobials	Isotretinoin, prior use of antimicrobials(moderate improvement) such as doxycycline, pristinamycin, rifampicin, zinc (no improvement), dapsone (no improvement), systemic corticosteroids (no improvement)	Isotretinoin, possible additional antimicrobials	Isotretinoin, previous treatment with broad-spectrum antibiotics, combination therapy of rifampicin + clindamycin
Treatment instructions	40–80 mg/day for 1–16 months	Give mean of 30 mg/day for unknown duration	0.5–0.8 mg/kg/day, average treatment length 3 months in 33 patients	N/A	1 mg/kg/day for at least 6 months, average of 9 months
Dosing	40-80 mg/day	Mean of 30 mg/day	0.5-0.8 mg/kg/day	Unknown	1 mg/kg/day
Treatment length average	Mean: 4.6 months <sup>a</sup> Range 1–16 months	Unknown	10 months <sup>a</sup>	N/A	9 months (6–18 months)
Cumulative dosing (mean, range in mg)	5731, 280–19,920	N/A	N/A	N/A	N/A
Follow-up (months)	29 (range: 6–84)	N/A	L <del>-</del> 9	N/A	N/A
Successful remission (%)	(75%, 12/16)	(88%)  or  (7/8)	(94.3%) or (33/35)	(80%) or (7/9)	(100%) or (4/4)
Recurrence rate (%)	(25%) or (4/16)	N/A	"Frequent relapse"	(22.2%) or $(2/9)$	"Recurrence did occur"
Family history	N/A	9.5%, 2/21 were related	None	N/A	N/A
Comorbidities	Acne conglobata (22.7%) or (15/66), none had pilonidal cysts	Crohn's disease (4.8%) or (1/21), acne conglobata (14.2%) or (3/21), hidradenitis suppurativa (23.8%) or (5/21), both hidradenitis suppurativa and acne conglobata (4.8%) or (1/21), none had pilonidal cysts	Hidradenitis suppurativa (12%) or (6/51), acne conglobata (16%) or (8/51), both hidradenitis suppurativa and acne conglobata (4%) or (2/21), none had pilonidal cysts	"Acne" (44.4%) (4/9)	None had association of acne conglobata or hidradenitis suppurativa (0/4)

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	Lee [9]	Segurado-Miravalles [5]	Badaoui [4]	Qi [8]	Tan [15]
Associated pruritis (%)	N/A	(90%) or (19/21)	(8%) or $(4/51)$	Yes, number not noted	N/A
Associated pain (%)	(55.7%)  or  (34/61)	(67%) or $(14/21)$	(25%) or (13/51)	Yes, number not noted	N/A
No. of nodules (1–5) (%)	(62.1%) or (41/66)	(71.4%) or $(15/21)$	N/A	N/A	N/A
No. of nodules $(>5)$ (%)	(37.9%) or (25/66)	(28.6%) or $(6/21)$	N/A	N/A	N/A
Bacterial culture results	Positive (CoNS) (46.2%) or (12/26), positive [ <i>Staphy-lococcus aureus</i> ] (15.4%) or (4/26), Positive [ <i>Enterobacter aerogenes</i> ] (3.8%) or (1/26), Positive [mixed bacteria] (11.5%) or (3/26), negative (23.1%) or (6/26), not done in 40 patients	Positive [Staphylococcus aureus] (28.6%) or (2/7), Positive [Staphylococcus epidermidis] (28.6%) or (2/7), negative (42.9%) or (3/7), not done in 14 patients	N/A	"Positive test" (11.1%) or (1/9)	N/A

CoNS coagulase-negative staphylococci, N/A data unable to be found within article aResults obtained from e-mailing the author

based on the z test were reported for all estimated efficacy. A p value of 0.05 was considered significant.

## 3 Results

## 3.1 Selection of Studies

A literature search returned 369 total articles, and 164 articles remained after de-duplication. Abstract and title review showed that of these 164 articles, 48 were case reports with fewer than three patients involved, three were not primary articles (one review article, one poster presentation, one abstract only), 12 merely discussed isotretinoin without administering it, and 92 discussed either isotretinoin or dissecting cellulitis but not both. These articles were excluded. Of the remaining articles, a full-text review revealed one article administered isotretinoin without mentioning treatment results, one article administered isotretinoin but not for dissecting cellulitis, one article administered isotretinoin and rifampicin together, and one article presented with an English abstract but the subsequent article was written in French. The remaining five articles were used for the purposes of this review. Because of unclear wording, two of the included articles had a possibility of administering isotretinoin concomitantly with another treatment [8, 9]. These studies were ultimately included because the possibility of concomitant treatment would have only affected a significant minority of their patient population that received isotretinoin. Reasons for exclusions were detailed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (Fig. 1).

## 3.2 Study Characteristics

The characteristics of the five studies are displayed in Table 1. All five studies were retrospective. The dates of publication were from 2004 to 2018, involving cases from 1995 to 2015. Studies were carried out in China (1), Taiwan (1), France (1), Spain (1), and Canada (1). The number of patients treated with isotretinoin had a range of 4–35. Patient age range was 12-62 years. Three studies listed the mean age of patients with DCS (mean: 26.7 years). The study participants were overwhelmingly male (144/153, 94.1%). Vertex of the scalp was the most commonly recorded location of nodules (range 49–89.4% of patients, mean: 99/138, 71.7%). Two studies cited the percentage of patients that had one to five scalp nodules (62.1% and 71.4%, mean: 56/87, 64.4%) and more than five scalp nodules (37.9% and 28.6%, mean: 31/87, 35.6%). Positive bacterial culture results were reported in three studies (25/42, 59.5%). No other laboratory results were reported in the data.

Table 1 (continued)

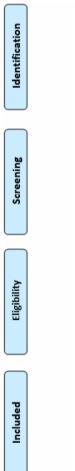
All studies used isotretinoin after prior use of oral antibiotics. One study mentioned combined use of isotretinoin and prednisolone in a few patients [9]. Isotretinoin dosing varied between studies. Some studies calculated isotretinoin dosing by body weight, between 0.5 and 1 mg/kg/day. One study administered isotretinoin in doses between 40 and 80 mg/day. One study administered 30 mg/day for all patients. Dosing was not defined in one study.

Treatment length range was 1–18 months. After contacting study authors, two studies defined mean treatment duration as 4.2 months and 10 months. One study defined mean treatment duration as 9 months but included other patients without DCS as well. Two studies did not provide values for mean treatment duration. Cumulative dosing was defined in only one study (mean 5731 mg; range 280–19,920 mg). Mean follow-up time was cited in two studies as 6–7 months and 29 months.

## 3.3 Summary Table of Findings

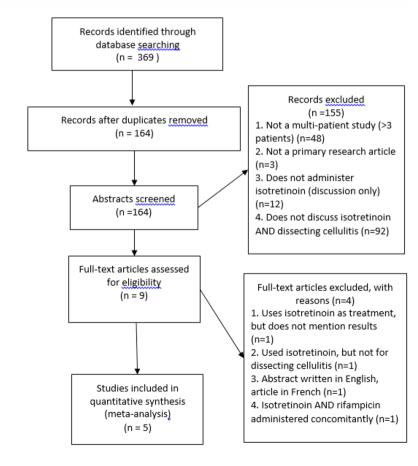
A summary of the findings is shown in Table 1.

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart of review



## 3.4 Efficacy

All five studies documented the percentage of patients that saw improvement of their dissecting cellulitis through use of isotretinoin. In all five studies, an overwhelming majority of patients saw improvement or complete remission of their dissecting cellulitis (75–100%). One study cited complete remission in a majority of patients (33/35, 94.3%) [4]. One study cited both complete remission (6/16, 37.5%) and partial improvement (6/16, 37.5%) in its patients [9]. One study cited reduction in inflammation in a majority of patients (7/8, 88%) [5]. Two studies did not elaborate on improvement [8, 15]. The combined percentage of patients who saw complete remission of disease was 76.5% (39/51). A pooled analysis of the five studies found high efficacy of isotretinoin in improving disease burden in patients with DCS. The overall efficacy of isotretinoin in treating DCS was estimated to be 0.9 with a 95% CI [0.81–0.97]. The study-specific and overall estimated efficacy are shown within the forest plot in Fig. 2. A sensitivity analysis was performed, and suggested that the overall efficacy of isotretinoin was still very high when excluding



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studies, with a range of 0.83–0.94. If the study with the largest sample size was removed, the estimated efficacy would be as low as 0.83 with a 95% CI (0.67–0.95). The sensitivity analysis is displayed in Table 2.

#### 3.5 Recurrence

Recurrence of dissecting cellulitis after treatment with isotretinoin was noted in four out of five studies. Each of the four studies defined recurrence as occurring after treatment discontinuation. Two of these studies did not give exact values on how many patients experienced recurrence. In the other two studies, the percentage of patients that had recurrences of DCS was 25% and 22.2%, with an overall recurrence of 24% (6/25). One study did not mention if recurrence had occurred or not. One study noted that re-treating dissecting cellulitis after recurrence led to "satisfactory" results [8].

## 3.6 Associated Manifestations

Four out of five studies cited an associated manifestation of acne conglobata from 14.2 to 44.4% of patients treated. One study cited no associated manifestation of acne conglobata. The total prevalence of acne conglobata was 18.5% (28/151). Two out of five studies cited an associated manifestation of hidradenitis suppurativa (12% and 23.8%). One study cited no associated manifestation of hidradenitis suppurativa, while two studies did not mention an associated manifestation of hidradenitis suppurativa. The total prevalence of hidradenitis suppurativa was 15.3% (11/72). Three studies cited no associated manifestation of pilonidal sinus, while two studies did not mention pilonidal sinus.

Two studies noted associated pruritus in patients (8% and 90%). One study noted associated pruritus in patients but did not give an exact number, while two studies did not mention

associated pruritus. The total prevalence of associated pruritus was 31.9% (23/72). Three studies noted associated pain with a range of 25–67% of patients. One study noted associated pain but did not give an exact number. One study did not mention associated pain. The total prevalence of associated pain was 45.9% (61/133).

## 4 Discussion

## 4.1 Summary of Evidence

This review found that isotretinoin is a highly effective treatment for providing improvement in dissecting cellulitis. The overall efficacy of isotretinoin for treating dissecting cellulitis was estimated to be 0.9 with a 95% CI (0.81–0.97). A consistently high proportion of patients saw improvement in their disease burden across all five studies, as demonstrated by the sensitivity analysis. Because of the variation in definitions of "efficacy" across studies,

Table 2 Sensitivity analysis of pooled efficacy rates

Study, year	Reported efficacy (95% CI)	Pooled efficacy after excluding one specific study (95% CI)
Lee [9]	0.75 (0.5–0.94)	0.94 (0.84–1)
Segurado- Miravalles [5]	0.88 (0.54–1)	0.91 (0.81–0.98)
Badaoui [4]	0.94 (0.84-1)	0.83 (0.67-0.95)
Qi [8]	0.78 (0.44-0.99)	0.92 (0.82-0.99)
Tan [15]	1 (0.61–1)	0.89 (0.79-0.96)

Fixed-effect models were used for pooled efficacy estimates *CI* confidence interval

**Fig. 2** Estimated efficacy rates of isotretinoin in treating dissecting cellulitis of the scalp. *CI* confidence interval

Study	Efficacy [95% CI]	N	Weight	Rate [95% CI]
Lee, 2018		16	9.34%	0.75 [0.50, 0.94]
Segurado-Miravalles, 2017		8	8.17%	0.88 [0.54, 1.00]
Badaoui, 2016	· •	35	65.23%	0.94 [0.84, 1.00]
Qi, 2014	•	9	5.70%	0.78 [0.44, 0.99]
Tan, 2004		4	11.56%	1.00 [0.61, 1.00]
Overall				0.90 [0.81, 0.97]
Heterogeneity: Q= 4.74 , p= 0.315				
0.40 0.50 0.60	0 0.70 0.80 0.90 1.00			

further statistical separation of efficacy based on degrees of improvement is not currently possible. However, the true proportion of patients who see a complete remission of disease after treatment should be significant, as two studies clearly defined a pool of patients as having "complete remission of disease", which would represent 54.16% (39/72) of patients included in these studies [4, 9]. While all studies reported prior use of antibiotics, one study included patients who did not respond to multiple prior treatments including antibiotics and oral corticosteroids [4]. The patients within this study may have had more severe disease. This did not seem to affect treatment response, as the patients in this study had a high percentage of "complete remission" (33/35, 92%). While there exists the possibility of concomitant therapy in a minority of patients in two studies, this did not correlate with treatment response as high rates of improvement were found in studies both with and without potential concomitant therapy [8, 9]. Future studies can improve the body of evidence by defining degrees of improvement, as well as comparing treatment with isotretinoin vs placebo or other treatments. Dosing varied throughout the five studies. However, the study with the most treatment success (33/35 patients had complete remission) used a dosage of 0.5-0.8 mg/kg/day with an average treatment length of 3 months [4]. Treatment length and cumulative dose should be recorded to see if there is a positive correlation with treatment response. While four out of five papers included average dosing, mean duration of treatment was reported in only two studies [4, 9]. Cumulative dosing average was cited in one study [9]. Without one of these two variables, it is difficult to accurately calculate whether the cumulative amount of isotretinoin administered correlates to better treatment outcomes. This information could greatly aid in standardizing current isotretinoin treatment guidelines for patients with DCS.

Study results suggest that recurrence is a commonly expected outcome after successful treatment of isotretinoin for dissecting cellulitis. Recurrence was noted in four out of five studies, although exact numbers were provided in only two studies (6/25, 24%). Retreatment with isotretinoin after recurrence seems to be a satisfactory option [8]. Recurrence of disease is also a commonly reported outcome across other treatment options such as oral antibiotics [4, 18]. Isotretinoin has been hypothesized to offer a longer duration of remission before disease recurrence [9]. Because of the lack of reporting of cumulative doses, it is not possible at this time to draw conclusions on whether higher cumulative doses can result in decreased recurrence. Maintenance therapy with 0.75–1 mg/kg/day has been described as a satisfactory option to combat the high

recurrence rates associated with DCS [19]. Future studies should also explore whether lower dosages of less than 0.5 mg/kg/day can be an effective option in reducing recurrence rates while minimizing potential side effects.

## 4.2 Associated Manifestations

Associated pain (61/133, 45.9%) and pruritus (23/72, 31.9%) were frequently documented symptoms, and are likely due to the inflammatory pathogenesis of DCS. Additionally, the mean age of onset (26.7 years), the predominance of nodules on the vertex of the scalp (99/138, 71.7%), and the overwhelmingly male patient population are consistent with what is described in the literature [4, 10]. Multiple scalp nodules are common, with over one-third of cited patients having more than five nodules (31/87, 35.6%). There was frequent mention of the associated manifestations of acne conglobata (30/151, 19.9%) and hidradenitis suppurativa (11/72, 18.5%), which are frequently described in the literature as part of the follicular tetrad along with dissecting cellulitis. These data show that these two diseases can occur concurrently with DCS. There was no mention of pilonidal cysts, with three studies explicitly mentioning that no patients had associated pilonidal cysts. This suggests that although DCS and pilonidal cysts are both parts of the follicular tetrad, they are not often found concurrently with each other. Bacterial cultures were commonly positive when reported (25/42, 59.5%). When positive, cultures grew coagulase-negative staphylococci, Staphylococcus aureus, Staphylococcus epidermidis, Enterobacter aerogenes, or mixed bacteria.

## 4.3 Limitations

The strengths of this study include the use of a comprehensive search strategy across five databases and the statistical analysis. The findings from this study are generalizable because the studies reported results from five different countries across three continents. This study has limitations owing to the low quality of study designs in the available literature. These include the lack of a control group to compare with isotretinoin, small study sizes, varied outcome measures, inconsistent dosages across studies, and reliance on observational studies instead of randomized controlled trials to analyze treatment efficacy. Future studies are required to answer whether isotretinoin is more effective than other common treatments for DCS. Inclusion of specific definitions for clinical improvement, dosage regimens, and recurrence rates would lead to more impactful conclusions to inform clinical practice. Use of prospective studies and larger sample sizes would help increase the quality of knowledge on treatments for dissecting cellulitis.

## 4.4 Implications for Practice

The findings from this review reveal that isotretinoin can be very effective as monotherapy for significant improvement or complete recovery of dissecting cellulitis. Oral antibiotics may still be considered as first-line therapy for less severe cases of dissecting cellulitis owing to their milder side-effect profile [9]. Recurrence after successful treatment of dissecting cellulitis is common, and subsequent retreatment with isotretinoin has been documented in the literature as successful [9]. Continued maintenance therapy with isotretinoin may help decrease the rate of recurrence [19]. The average dosing requirement amongst these five studies was 0.5–0.75 mg/kg/day for a minimum of 3 months.

## 4.5 Treatment Alternatives

There is no well-established treatment for dissecting cellulitis that is refractory to antibiotics and isotretinoin [10]. Surgical excision of sinus tracts can be done but is very destructive [20].

Tumor necrosis factor-α inhibitors, adalimumab and infliximab, have been detailed in case studies to be effective in improving DCS [21–26]. One case report notes that of the 14 patients who have been described in case reports (as of 4 July, 2019), 85.7% (12/14) saw an improvement in inflammatory skin symptoms of DCS. After not responding to treatment with isotretinoin, 71.4% (10/14) were administered tumor necrosis factor- $\alpha$  inhibitors [21]. The most common dosage used for adalimumab was an 80-mg loading dose with a 40-mg dose every other week thereafter, while the most common dosage used for infliximab was 5 mg/kg at 8-week intervals [21]. Complete remission was seen in three patients [23, 26, 27]. One study noted that in two out of three patients, inflammatory infiltrate was reduced but the underlying subcutaneous sinus tract structure stayed unchanged, and one patient relapsed 4 weeks after cessation of treatment [24]. It seems that while tumor necrosis factor- $\alpha$  inhibitors may be effective in improving DCS in patients who have not responded to or who cannot take isotretinoin, it may not be a curative option. Biologic agents are known to only suppress the underlying inflammatory process, and upon cessation would likely lead to disease relapse.

There have been three recent case studies detailing the use of multiple sessions of 10% aminolevulinic acid during photodynamic therapy (ALA-PDT) laser treatment as an alternative to isotretinoin [28–30]. These studies have cited significant improvement or complete remission in patients with DCS at an efficacy comparable to isotretinoin [28–30]. No recurrence was cited in two studies (follow-up at 7 weeks [30] and 3 months [28]). Treatment with 10% ALA-PDT

may also be a safe alternative for dissecting cellulitis that is refractory to isotretinoin, patients who have adverse effects from using isotretinoin (acne fulminans [31], pseudotumor cerebri [32], hepatotoxicity [33]), alcoholics [33], or pregnant women [34]. It is also an attractive option in that it may offer a lower rate of recurrence than isotretinoin [28, 30]. However, more data are needed.

## 5 Conclusions

Isotretinoin is a highly effective treatment for improving symptoms of dissecting cellulitis of the scalp. Disease recurrence is a common finding for those who undergo successful treatment, and subsequent retreatment with isotretinoin is an option. It will be important for future studies to document follow-ups, duration of treatment, average dosing, and average cumulative dose to draw conclusions on clinical dosing guidelines.

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## **Declarations**

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Conflicts of Interest/Competing Interests William Guo, Chencan Zhu, Gregg Stevens, and David Silverstein have no conflicts of interest that are directly relevant to the content of this article.

Ethical approval The study conducted was in accordance with the ethical standards of the 1964 Helsinki declaration and subsequent amendments.

Availability of Data and Material Not applicable.

Code availability Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

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