Is Etanercept Effective for Hidradenitis Suppurativa?

Treatment of Hidradenitis Suppurativa With Etanercept Injection.

Adams DR, Yankura JA, et al:

Arch Dermatol 2010; 146 (May): 501-504

Etanercept injections do not appear to result in significant improvement of hidradenitis suppurativa.

Background: Hidradenitis suppurativa is a chronic skin disease that carries significant morbidity. Patients suffer from recurrent nodule formations, abscesses, fistulas, and scarring. Finding an effective treatment of hidradenitis suppurativa has been challenging. Clinicians have used antibiotics, retinoids, antiandrogens, immunosuppressive agents, lasers, and/or surgical interventions with varying success. Etanercept is a dimeric human tumor necrosis factor (TNF) receptor approved for the treatment of moderate to severe psoriasis, psoriatic arthritis, rheumatoid arthritis, juvenile idiopathic arthritis, and ankylosing spondylitis. Two small, uncontrolled prospective studies had shown a clinically significant benefit of etanercept in hidradenitis suppurativa, thereby evoking the question of whether high-dose etanercept 50 mg twice weekly would be effective for hidradenitis suppurativa in a randomized, controlled trial.
Objective/Design: To evaluate the effects of etanercept treatment on hidradenitis suppurativa in a randomized, double-blind, placebo-controlled study.
Methods: The authors included 20 patients with hidradenitis suppurativa and randomized them to receive either subcutaneous etanercept 50 mg twice weekly or subcutaneous placebo twice weekly for 12 weeks. After these 12 weeks, the participants entered an open-label phase, in which the placebo group crossed over to receiving etanercept, and all participants received etanercept 50 mg twice weekly from weeks 13 through 24. The primary end point was whether hidradenitis suppurative achieved a "clear" or "mild" status at week 12 per the physician global assessment. The secondary end points included patient global assessment of hidradenitis suppurativa lesions, associated pain, and Dermatology Life Quality Index.
Results: The investigators did not observe statistically significant differences in physician global assessment between the treatment and placebo groups at 12 and 24 weeks. They also did not observe significant differences in physician-assessed pain, erythema, or discharge between the 2 groups. Furthermore, there were no statistically significant differences between the 2 study arms in the patient global assessment, pain level, or quality of life at weeks 12 or 24.
Conclusions: Subcutaneous etanercept 50 mg twice weekly did not have significant efficacy in the treatment of hidradenitis suppurativa.
Reviewer's Comments: While applying anti-TNF therapy for non-psoriatic dermatologic indications seems attractive, we need to interpret anecdotal experiences in the literature with caution. This is the first double-blind, placebo-controlled study that examined 50-mg twice-weekly etanercept therapy in hidradenitis suppurativa for up to 24 weeks. The negative results from this long-awaited trial are important to include in the literature, and these findings direct researchers' attention toward investigating long-term efficacy of 2 other anti-TNF agents, infliximab and adalimumab. (Reviewer-April W. Armstrong, MD).

Keywords: Hidradenitis Suppurativa, Etanercept, Anti-TNF Agents

Print Tag: Refer to original journal article

Technique Effective for Axillary Osmidrosis

Effectiveness and Complications of Subdermal Excision of Apocrine Glands in 206 Cases With Axillary Osmidrosis.

Qian JG, Wang XJ:

J Plast Reconstr Aesthet Surg 2010; 63 (June): 1003-1007

Consider subdermal excision for the treatment of axillary osmidrosis or hyperhidrosis.

Background: Osmidrosis is a condition of excessive axillary malodor. It is primarily of concern to patients residing in East Asia, unlike the west where the primary concern is hyperhidrosis. Although the cause of osmidrosis is thought to be excessive apocrine gland secretion rather than excessive eccrine activity, the treatment of osmidrosis and hyperhidrosis is similar.
Objective: To present the results of an updated subcutaneous glands excision technique.
Participants/Methods: 256 consecutive patients were treated from 2005 to 2008. Follow-up was available for 206 patients, ranging from 3 to 40 months. Data were recorded using a specially designed form. A 3-cm incision was made on the axillary crease after infiltration with tumescent solution. The area was undermined, the underside of the skin was defatted, and the glands were excised under loop magnification. A drain was placed for 24 hours. The incision site was closed primarily after excision of the subdermal tissue.
Results: The mean age was 23.4 years, and the female-to-male ratio was 131:75. Of the patients studied, 183 had a family history of the disorder, and 16 had concurrent hyperhidrosis. Malodor elimination was judged good in 97%, fair in 3%, and poor in 0%; 95% of patients were totally satisfied with the technique, 4% were partially satisfied, and 0.5% were regretful. Ninety-five percent of patients had >75% hair reduction, and 5% had 50% to 75% reduction. All patients reported a significant reduction in axillary sweating; 37% reported superficial epidermal necrosis, and 3.6% had pressure blisters at the shoulder. The rate of other complications was very low; 5.1% of subjects had wound dehiscence.
Conclusions: Success rates from this procedure were very high and complication types were mostly minor and low in frequency. This technique should be the surgical treatment of choice for this condition.
Reviewer's Comments: This is one of many techniques advocated for the treatment of both osmidrosis and hyperhidrosis. These techniques use diverse methodologies including liposuction abrasion, curettage, laser ablation, and outright excision. All modalities have as their goal the destruction of subdermal tissue containing eccrine and apocrine glands. Success rates vary, but most studies report positive outcomes. These techniques are commonly performed by dermatologists. This particular technique does not require the acquisition of expensive liposuction or laser equipment and should be easy to perform. I wonder if the incision was made in the inferior rather than superior axillary vault and allowed to heal by second intention rather than primary closure, and whether this would obviate the need for placement of a drain that requires a second patient visit. (Reviewer-Daniel Eisen, MD).

Keywords: Osmidrosis, Surgery

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Number of Exams Not Related to Survival for Stage III Melanoma

Site and Timing of First Relapse in Stage III Melanoma Patients: Implications for Follow-Up Guidelines.

Romano E, Scordo M, et al:

J Clin Oncol 2010; 28 (June 20): 3042-3047

Routine imaging and blood work are probably not necessary for stage III melanoma patients.

Background: Guidelines regarding follow-up for stage III melanoma have largely been anecdotal.
Objective/Methods: This was a retrospective review of stage III melanoma patients with no evidence of disease who eventually relapsed between 1992 and 2004. The following data were collected: date of first relapse, time to first relapse, method of first relapse detection, and survival. The 5-year relapse-free survival rate was also calculated. Standard follow-up for these patients was performed every 3 months after diagnosis for 2 years, then every 6 months. CT scans, CBC, lactate dehydrogenase (LDH), and comprehensive metabolic panels were typically performed before each follow-up.
Results: Local/in-transit metastases accounted for 28% of relapses, regional nodal metastases for 21%, and systemic metastases for 51%. The patient or family detected 47% of recurrences, physicians detected 21%, and radiologic tests detected 32%. The 5-year relapse-free survival rate was calculated at 63% for stage IIIA, 32% for stage IIIB, and 11% for stage IIIC. All local/in-transit relapses for stage IIIA occurred by 40 months, but systemic recurrence occurred as late as 71 months. For stage IIIC patients, all recurrences happened by 2 years. Elevated LDH was the presenting sign in only 1.2% of recurrences; other blood tests were unhelpful. Months of progression-free survival and number of oncology, surgical, or dermatologic visits did not correlate with the probability of discovering a resectable relapse.
Conclusions: Routine examinations >3 years after diagnosis for stage IIIA, 2 years for stage IIIB, and 1 year for stage IIIC patients will detect few systemic relapses. Radiologic imaging >3 years after diagnosis for stages IIIA and IIIB and 2 years for stage IIIC patients will also detect few recurrences.
Reviewer's Comments: Since the probability of detecting relapses with physical exam beyond 3 years for stage IIIA, 2 years for stage IIIB, and 1 year for stage IIIC are <5%, I agree with the authors that intensive follow-up visits are unnecessary beyond these time intervals. Of interest is that the study failed to show an association between the number of screening visits and overall survival. This likely reflects the very poor efficacy of our adjuvant therapies for melanoma. One could make the argument against any follow-up for stage III melanoma based on these results, although I will not be putting myself in that camp just yet. The value of screening CT scans remains debatable, although there is good evidence now that they can be completely discarded for asymptomatic patients >3 years out from their initial diagnosis for stage IIIA and IIIB and 2 years for stage IIIC disease. Routine brain scans appear to be completely useless except for perhaps stage IIIC patients during the first year. (Reviewer-Daniel Eisen, MD).

Keywords: Melanoma, Imaging, Physical Exam, Screening, CT, CBC, MRI, LDH

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Topical Capsaicin Effect Varies by Ethnicity

Ethnic Differences in Pain, Itch and Thermal Detection in Response to Topical Capsaicin: African Americans Display a Notably Limited Hyperalgesia and Neurogenic Inflammation.

Wang H, Papoiu ADP, et al:

Br J Dermatol 2010; 162 (May): 1023-1029

Post-capsaicin warmth thresholds increase for African Americans and decrease in Hispanics, who also experience increased pruritis.

Background: One of the most useful spinoffs of the genomics revolution over the past decade has been an increased understanding of the polymorphisms that determine response to therapeutic drugs. There are personal as well as ethnic differences in response to medications—in fact, we've learned to expect them. One drug that shows a significant variation in effectiveness from person to person is capsaicin, an analgesic drug used for the treatment of pain, including pain from peripheral neuropathy.
Objective: To evaluate ethnic variations in noxious stimulus detection after treatment with topical capsaicin.
Participants: 40 healthy subjects: 10 African Americans, 10 East Asians, 10 Hispanics, and 10 Caucasians. None of the individuals except one Hispanic subject was reported to consume a large amount of chili peppers.
Methods: The authors measured warmth sensation and heat pain detection thresholds and pain intensity before and after application of capsaicin or placebo on the forearms. The device used was a standard commercial quantitative thermosensory testing system. This system uses a 12 cm2 probe that warms the skin at a rate of 0.4°C per second up to 50°C. The subjects reported warmth sensation threshold followed by heat pain detection threshold. Pain was also reported after capsaicin or placebo application using a 0 to 100 pain intensity scale. Any nonpainful sensations were also recorded. The investigators measured skin blood flow with a laser Doppler device, and any positive skin flare response was measured visually with a ruler.
Results: In African Americans, the heat pain detection threshold, pain intensity, and skin blood flow did not change significantly after capsaicin application. However, in the other 3 groups, there was significant hyperalgesia and vasodilatation. The post-capsaicin warmth sensation threshold increased in African Americans and decreased in Hispanics. Hispanics also uniquely experienced post-capsaicin itch.
Conclusions: African Americans displayed significantly reduced pain hypersensitivity after topical capsaicin compared to the 3 other ethnic groups.
Reviewer's Comments: Several previous studies have shown differences in pain thresholds among ethnic groups, with most suggesting that African Americans generally have a decreased tolerance to pain stimuli, a lower thermal pain tolerance, and higher ratings of unpleasantness and intensity to thermal stimuli compared to Caucasians. This study showed that topical application of capsaicin was an exception. Although African Americans had no change in heat pain detection, the warm sensation threshold was increased. Therefore, this study still begs the question of whether capsaicin would be a more useful drug in African Americans for neuropathic pain and itch than in other ethnic groups; it certain suggests it would be better tolerated. Until there is further study, since capsaicin is safe, it seems reasonable to offer it as an optimistic therapeutic choice, especially for African Americans. (Reviewer-David L. Swanson, MD).

Keywords: Capsaicin, Pain, Ethnicity, Neuropathy

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TNF Antagonists in Psoriasis Have High Benefit-Risk Ratios

Benefit-Risk Assessment of Tumour Necrosis Factor Antagonists in the Treatment of Psoriasis.

Langley RG, Strober BE, et al:

Br J Dermatol 2010; 162 (6): 1349-1358

Etanercept, infliximab, and adalimumab all have high benefit-to-risk ratios in patients with psoriasis.

Background: Tumor necrosis factor (TNF) antagonists are so mainstream now that we are all quite comfortable prescribing them for our psoriasis patients. However, we also acknowledge the potential risk of noninfectious and infectious adverse events from these drugs. How great is that risk? One way to report and understand risk is as a percentile probability. Another way is to calculate the risk-benefit ratios as a function of the number needed to treat (NNT) for efficacy versus number needed to harm (NNH). Another method is through calculation of the number of patient-years of treatment that would be expected to result in a sentinel event.
Objective: To determine the benefit versus risk for adalimumab, etanercept, and infliximab in the treatment of psoriasis.
Design: Comprehensive literature review with data analysis.
Methods: The authors integrated data from the published literature and posters presented at national, regional, and international dermatology congresses. For the NNT analysis, they used various efficacy measures such as the Physician's Global Assessment and Psoriasis Area and Severity Index (PASI 75) scores. The authors also looked at corresponding data of the percentages of patients reporting adverse events, serious adverse events, and selected adverse events of special interest.
Results: The authors found that the NNT for PASI 75 was 1.6 for adalimumab 40 mg every other week, 3.2 for etanercept 50 mg weekly or 25 mg twice weekly, 2.3 for etanercept 50 mg twice weekly, and 1.4 for infliximab 5 mg/kg. For serious noninfectious, serious infectious, and malignant adverse events, the estimated NNH was at least 2 orders of magnitude greater and several orders of magnitude greater for events of serious toxicity. The number of patient-years of observation necessary to detect an event were 56 to 73 for serious infection, 164 to 507 for malignancy excluding skin cancer, and 818 to 1286 for congestive heart failure.
Conclusions: The likelihood of treatment success for these agents far exceeds the likelihood of serious harm.
Reviewer's Comments: I always run through the litany of risks of these drugs with patients. It is reassuring to be able to tell them that typically one might expect to have to wait a millennium, for example, for any likelihood of drug-related congestive heart failure to be observed in any given patient (although that somewhat misrepresents the meaning of the statistic). (Reviewer-David L. Swanson, MD).

Keywords: Psoriasis, Etanercept, Infliximab, Adalimumab

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How to Differentiate Between Primary Cutaneous Tumors and Adenocarcinomas Metastatic to the Skin

Value of p63 and Podoplanin (D2-40) Immunoreactivity in the Distinction Between Primary Cutaneous Tumors and Adenocarcinomas Metastatic to the Skin: A Clinicopathologic and Immunohistochemical Study of 79 Cases.

Plaza JA, Ortega PF, et al:

J Cutan Pathol 2010; 37 (April): 403-410

The combination of p63 and podoplanin (D2-40) can assist with the differentiation between primary cutaneous tumors and adenocarcinomas metastatic to the skin.

Background: The morphological distinction between primary cutaneous neoplasms and adenocarcinomas metastatic to the skin continues to be a challenging diagnostic problem. Morphological criteria are now assisted with a wide array of immunohistochemical stains. However, even with these additional assays, in the absence of a known primary visceral malignancy, an absolute diagnosis may still be elusive.
Objective: Immunohistochemical stains for p63 and podoplanin (D2-40) were utilized to determine whether primary cutaneous tumors can be differentiated from metastatic adenocarcinomas to the skin.
Design: Retrospective review.
Participants: 37 primary cutaneous carcinomas (mixture of benign and malignant adnexal tumors and skin epithelial carcinomas) and 42 metastatic carcinomas (breast, gastrointestinal tract, kidney, lung, and endometrium) were examined.
Methods: Routine H&E stains and immunohistochemical stains for podoplanin and p63 were performed on all tumors. All metastatic tumors had a well-documented and biopsy-proven primary tumor. The distribution and intensity of staining were graded for each stain.
Results: Podoplanin was positive in nearly all adnexal neoplasms and cutaneous carcinomas (34 of 37) and was negative in all metastatic carcinomas; p63 was positive in all adnexal neoplasms and cutaneous carcinomas (37 of 37) and negative in all metastatic carcinomas. These results were statistically significant (P <0.0001) with a positive and negative predictive value of 100% for both immunostains.
Conclusions: The combination of p63 and podoplanin (D2-40) can assist in the differentiation between primary cutaneous tumors and adenocarcinomas metastatic to the skin.
Reviewer's Comments: This excellent study examines a wide spectrum of primary cutaneous neoplasms and metastatic adenocarcinomas to the skin. A strength of this study is the inclusion of several primary adnexal carcinomas such as eccrine carcinomas, which may mimic metastatic adenocarcinomas both by morphology and by immunohistochemistry. Podoplanin was less sensitive and specific than p63, but both stains should be utilized since staining may be focal. This may be troublesome if the diagnostic biopsy is small with not much tumor to identify. I have utilized this combination of stains in my own practice and have found consistency with this study, differentiating primary eccrine carcinomas from known metastatic breast and colon carcinomas. I look forward to the inclusion of additional primary cutaneous tumors and metastatic adenocarcinomas to expand the diagnostic utility of these 2 immunohistochemical stains. (Reviewer-Paul K. Shitabata, MD).

Keywords: Dermatopathology, Immunohistochemistry, Metastatic Adenocarcinoma, Skin Cancers

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Determining Origin of Perniosis

Perniosis: Clinical and Histopathological Analysis.

Boada A, Bielsa I, et al:

Am J Dermatopathol 2010; 32 (February): 19-23

Skin biopsy is not necessary for a diagnosis of perniosis as it cannot discriminate between idiopathic and autoimmune etiologies.

Background/Objective: The authors present 20 biopsy-proven cases of perniosis diagnosed between 1988 and 2007 at a single institution in Barcelona, Spain. The main objective of their study was to try to classify the cases as either idiopathic or associated with an autoimmune disorder, mainly systemic lupus erythematosus (SLE).
Methods/Participants: There were 11 patients (10 female, 1 male) with autoimmune perniosis. In 7 patients (64%), perniosis presented before the autoimmune disorder. The mean age was 29.9 years (range, 14 to 61 years).
Results: 10 patients had lupus, and 1 had Sjögren syndrome. Of the 10 patients with lupus, 8 had chronic cutaneous lupus erythematosus (CLE) and 2 had subacute CLE. One patient with subacute CLE and 1 patient with CLE met criteria for SLE. Histologically, the most important features were peri-eccrine distribution of lymphocytes and dermal edema in idiopathic perniosis, spongiosis, vacuolation of the basal layer, and fibrin deposition in autoimmune perniosis.
Conclusions: The only feature that reached statistical significance was the peri-eccrine distribution of the inflammatory infiltrate in idiopathic cases.
Reviewer's Comments: A few weeks ago, I saw an 18-year-old healthy female patient with mildly painful purple lesions on her toes. She denied symptoms suggestive of collagen tissue disorder or risk factors for hepatitis. The question was whether I should investigate an autoimmune disorder in this patient. This article tells me I should, if not for anything else, because >64% of cases of autoimmune perniosis presented before their lupus. The performance of a skin biopsy, however, is more controversial because there are no specific features diagnostic of autoimmune perniosis. The point is that, at the end, it is the clinician who has to decide on clinical grounds alone if the patient should undergo a work-up for autoimmune disorders. If that is the case, the currently recommended work-up for patients with perniosis includes a thorough history and physical exam, sedimentation rate, CBC, antinuclear antibodies (ANAs), complement levels, and cryoglobulins. A skin biopsy is not necessary, as it contributes little in most cases. An association with SLE is likely when patients develop numerous episodes of perniosis, a longer duration until resolution, Raynaud's phenomenon, pathologic changes in nail capillaroscopy, and positive ANAs and anti-SSA/Ro. Additionally, the literature suggests that fingertip ulcerations and frequent episodes of perniosis outside winter season occur more frequently in lupus-associated perniosis. (Reviewer-Carlos Garcia, MD).

Keywords: Perniosis, Chilblains, Systemic Lupus Erythematosus

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Are Antimalarials Effective in SLE?

Antimalarial Treatment May Have a Time-Dependent Effect on Lupus Survival: Data From a Multinational Latin American Inception Cohort.

Shinjo SK, Bonfá E, et al:

Arthritis Rheum 2010; 62 (March): 855-862

In this study, the use of antimalarials for >6 months in lupus patients was associated with a 38% reduction in mortality rate, independent of patient's age or ethnicity.

Design: The authors performed an observational inception cohort study as part of the Grupo Latino Americano de Estudio del Lupus Eritematoso (GLADEL) lupus cohort at 34 centers in 9 Latin American countries.
Objective: (1) To determine cause of death in patients with lupus as related to active disease, cardiovascular or thrombotic complications, infection, and/ or cancer; and (2) to investigate the relationship between antimalarial use and survival.
Methods: At the time of the study, the GLADEL cohort included 1480 patients. Of these, 1141 (77%) were antimalarial users, and 339 patients (23%) were nonusers. The mean antimalarial exposure time for users was 48.5 months (range, 6 to 98 months). Eighty percent of patients had been taking the medication for >2 years.
Results: There was a statistically significant difference in mortality rate between groups. The mortality rate was 4.5% for antimalarial users and 11.5% for non users.
Conclusions: "Antimalarial drugs were shown to have a protective effect, possibly in a time-dependent manner, on systemic lupus erythematosus (SLE) survival. These results suggest that the use of antimalarial treatment should be recommended for patients with lupus."
Reviewer's Comments: In this study, the use of antimalarials for >6 months was associated with a 38% reduction in mortality rate, independent of patient age or ethnicity. The survival of patients with systemic lupus has improved over time; currently, the 20-year survival is close to 70%. Mortality is determined primarily by poverty, disease activity, and organ damage. Although several experts now propose the use of antimalarials in most patients with lupus (independent of clinical manifestations), it is reasonable to question this approach and consider data from large-population studies using various lupus indexes that document organ damage since the onset of lupus. Some of the most widely reported include damage due to comorbid disease, therapy, and/or disease activity. High scores are associated with mortality, and early organ damage can be used as a prognostic factor. Previous studies have suggested that renal damage, renal failure, and pulmonary disease significantly predict mortality within 10 years regardless of therapy. Also, there appears to be a difference in survival among various ethnic groups. For example, Afro-Caribbean and Asian patients have a significantly higher severity of renal disease and a lower survival rate. In summary, the data supporting a survival benefit with antimalarial use are interesting and compelling, but the issue is still unresolved. (Reviewer-Carlos Garcia, MD).

Keywords: Antimalarials, Systemic Lupus Erythematosus, Survival, Mortality

Print Tag: Refer to original journal article

Treatment of Melanoma In Situ -- Decisions, Decisions

Treatment Options in Melanoma In Situ: Topical and Radiation Therapy, Excision and Mohs Surgery.

Erickson C, Miller SJ:

Int J Dermatol 2010; 49 (May): 482-491

Radiation therapy is a good alternative for treatment of melanoma in situ in poor surgical candidates.

Objective: To review the literature to evaluate the effectiveness of various techniques for the treatment of melanoma in situ (MIS).
Background: In the United States, surgical excision with 5-mm margins has been the standard of care for melanoma in situ, although different variations of Mohs surgery are often used to treat ill-defined lesions. Radiation is used less often, and imiquimod has been proposed more recently, primarily in small case reports. However, controversies exist with all these approaches.
Design/Methods: The authors performed a PubMed literature search using the following terms: imiquimod, radiation therapy, excisional surgery, and Mohs surgery. Articles pertaining to the treatment of melanoma in situ were reviewed and reported.
Results: Cure rates for the various therapies were as follows: (1) imiquimod, 75%; (2) radiotherapy, 85%; (3) surgical excision with 5-mm margins, 80% to 94%; and (4) Mohs surgery, 95% to 98%.
Conclusions: Imiquimod therapy seems to provide fairly low cure rates for MIS. However, because some of these lesions “contain an unrecognized invasive component,” imiquimod should be with used with caution. Radiation may be useful if surgery is not indicated.
Reviewer's Comments: The current standard of care for MIS is excision with 5-mm margins. This approach has significant limitations. First, there is a 20% chance of missing an invasive melanoma component when performing punch or incisional biopsies. Second, excision of large lesions in the face carries important cosmetic consequences. Third, the risk of developing invasive melanoma from a lentigo maligna is not known. Last, many patients with MIS are elderly and are poor surgical candidates. For all these reasons, alternative therapies are needed. This paper suggests that imiquimod is not a very good option. The most solid scientific evidence showed a 75% cure rate after 3 months of daily application of imiquimod. Radiation therapy is an effective alternative to surgery in poor surgical candidates. This approach is successful in at least 85% of cases, but the number of patients treated so far is very low. Surgical excision with 5-mm margins results in 6% to 20% recurrence. If possible, the surgical margins should be increased to 9 mm for lesions <2 cm in diameter and 1.2 cm for those >2 cm. Mohs surgery is the most effective therapy, but there is a significant learning curve. Results can be improved with the use of immunohistochemistry stains or paraffin- embedded sections. (Reviewer-Carlos Garcia, MD).

Keywords: Melanoma In Situ, Lentigo Maligna, Imiquimod, Mohs Surgery, Surgical Excision, Radiation

Print Tag: Refer to original journal article

Is Isotretinoin Associated With IBD?

Isotretinoin Use and the Risk of Inflammatory Bowel Disease: A Case–Control Study.

Crockett SD, Porter CQ, et al:

Am J Gastroenterol 2010; March 30 (): epub ahead of print

This case-control study suggests an association between isotretinoin use and ulcerative colitis.

Background/Objective: Several case reports have suggested an association between isotretinoin use and the subsequent development of inflammatory bowel disease (IBD). The potential link is based primarily on case reports describing the development of IBD during or in the 12 months after isotretinoin use. These reports have resulted in changes to the labeling for isotretinoin to indicate a possible IBD risk and in successful lawsuits against Roche Pharmaceuticals. The one published case-control study did not demonstrate an association between IBD and isotretinoin.
Methods: Case-control study using a large insurance database from the United States. The authors identified 8189 cases of IBD and 21,832 age-, gender-, and health insurance plan-matched controls. The outcome measure evaluated was the incidence of isotretinoin use in the 12 months before diagnosis of IBD.
Results: 24 of 8189 IBD subjects and 36 of the 21,832 control subjects were exposed to isotretinoin within the 12 month before diagnosis. Isotretinoin exposure was 4.36-fold more common in ulcerative colitis (UC) than in control subjects. In contrast, Crohn's disease (CD) did not show a statically significant association with isotretinoin. Increasing doses and exposure times were associated with a greater risk of UC.
Conclusions: The authors suggest that UC, but not CD, is associated with isotretinoin exposure, although the absolute risk of developing UC after isotretinoin use is very small.
Reviewer's Comments: Although isotretinoin is a uniquely effective acne treatment, it has become a lightning rod for personal injury lawsuits. Given that IBD is associated with Hidradenitis suppurativa (an acne-related disease) UC might be associated with severe acne rather than isotretinoin itself. The authors claim that their database indicates no relationship between acne and IBD but did not consider the severity of the acne. Although this study requires confirmation and better demonstration of causality, I think it is reasonable to warn patients of the potential IBD risk before starting isotretinoin. (Reviewer-Michael S. Kolodney, MD, PhD).

Keywords: Isotretinoin, Inflammatory Bowel Disease

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Consider Intralesional Chemotherapy for Classic KS

Intralesional Vincristine as First-Line Therapy for Nodular Lesions in Classic Kaposi Sarcoma: A Prospective Study in 151 Patients.

Brambilla L, Bellinvia M, et al:

Br J Dermatol 2010; 162 (April): 854-859

Classic Kaposi sarcoma responds to intralesional vincristine.

Background: Kaposi sarcoma (KS) is an angioproliferative neoplasm associated with human herpes virus 8 infection. It was originally described in elderly men of Mediterranean ethnicity (classic KS), but is now most commonly associated with HIV infection. A variety of treatments are used to control KS, including topical retinoids, surgery, radiotherapy, cryotherapy, and intralesional injection with interferon or chemotherapy agents. Although the advanced stages of KS may require systemic chemotherapy, most patients present with nodular disease that requires only local therapy to prevent pain, bleeding, or disfigurement.
Objective: To determine the efficacy of intralesional vincristine for nodular lesions of classic KS.
Design: Prospective open-label clinical trial.
Participants: 151 Italian patients with classic KS.
Methods: The investigators chose a target lesion and a control lesion on a lower limb of each subject. They injected 0.03 to 0.08 mL of vincristine (1 µg/mL) into the target KS nodule. Adverse events were assessed after 1 week, and efficacy was determined at 4 and 12 weeks.
Results: 76% of treated lesions and 4.6% of control lesions completely resolved by 12 weeks; 18% of lesions showed partial response (defined as >50% reduction in size). One patient showed no response, and the injected lesion increased in size in 1 patient. Adverse events occurred in 13.9% of patients and consisted mainly of burning, itching, and erythema. However, 2% of subjects experienced severe pain or ulceration.
Conclusions: The authors suggest that intralesional vincristine may be used as a first-line treatment for nodular KS.
Reviewer's Comments: Vincristine is a plant-derived microtubule-inhibiting alkaloid used as systemic chemotherapy for a variety of hematologic malignancies. Its use is limited by a tendency to cause peripheral neuropathy. The intralesional dose in this study is about 1/10,000 of the systemic dose used for chemotherapy. The reported response rate is impressive, and the side effects are relatively mild. Although the possibility of neurotoxicity is still a concern, the lack of systemic effects seen in this study and the small dose used suggest that vincristine is a cost effective, highly effective therapy for nodular classical KS. Although HIV-associated KS is caused by the same virus as classic KS, it is unclear if vincristine is equally effective for this more common form of the disease. (Reviewer-Michael S. Kolodney, MD, PhD).

Keywords: Vincristine, Kaposi Sarcoma

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