Topical combined 5-fluorouracil and calcipotriene for actinic keratosis and superficial keratinocyte carcinoma: Modified Delphi expert panel recommendations from ITSCC

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Background: Evidence on topical combined 5-fluorouracil/calcipotriene (5-FU/C) treatment of actinic keratoses (AKs), squamous cell carcinoma in situ (SCCIS), and superficial basal cell carcinoma is lacking.

Objective: To develop an expert consensus regarding 5-FU/C treatment of AKs, SCCIS, and superficial basal cell carcinoma.

Methods: Expert panelists were provided 5-FU/C literature review findings and survey results from International Immunosuppression and Transplant Skin Cancer Collaborative clinician members who prescribe 5-FU/C.

Results: Nine dermatologist/dermatologic surgeon International Immunosuppression and Transplant Skin Cancer Collaborative members with >5 years post-training experience or considerable clinical experience prescribing 5-FU/C participated in the panel. A 70% or higher concordance among respondents represented consensus. Key recommendations include: treating AKs with 5-FU/C twice daily for 4 to 5 days on the face/neck and 7 to 10 days on the scalp, trunk, and extremities; treating SCCIS with 5-FU/C twice daily for 7 to 10 days on the face/neck and 10 to 14 days on the scalp, trunk, and extremities; treating actinic cheilitis with 5-FU/C twice daily for 4 to 5 days; and no treatment modifications for patient immunosuppression.

Limitations: Small panel size and literature to date primarily including small, retrospective studies.

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Conclusions: Dermatologists may consider implementation of expert panel recommendations for treatment of AKs, SCCIS, and sBCC with 5-FU/C while awaiting larger, high-quality studies. (J Am Acad Dermatol 2026;95:112-20.)

Key words: 5-fluorouracil; 5-FU; actinic keratosis; basal cell carcinoma; calcipotriene; chemotherapy; combination; field therapy; squamous cell carcinoma in situ; topical; treatment; vitamin D.

CAPSULE SUMMARY

- Evidence for 5-fluorouracil/calcipotriene treatment of actinic keratoses and superficial keratinocyte carcinomas is promising, but a lack of clear recommendations likely limits broader use.
- Consensus recommendations based on current literature and expert experience aim to clarify indications and prescription practices while highlighting potential areas for future research.

INTRODUCTION

Topical therapies are central to the management of actinic keratoses (AKs) and superficial keratinocyte carcinomas (SKCs). Among FDA-approved AK treatments, 5-fluorouracil (5-FU) is one of the most effective, yielding clearance rates ranging from 42.9% to 76.6%, fewer AKs than in controls 6 months posttreatment, and decreased treatment failure compared to other topical therapies.[1-3] 5-FU is also used for SKCs, including squamous cell carcinoma in situ (SCCIS) and superficial basal cell carcinoma (sBCC).[4,5] Though only FDA-approved for sBCC, 5-FU achieves clearance rates up to 80% to 90% for sBCC and 85% for SCCIS.[6,7] Surgical management has a modest but statistically significant advantage over topicals in 5-year recurrence-free survival.[8] However, topical management remains highly effective and may be preferred for patient convenience, poor surgical candidates, high tumor burden, or extensive, confluent actinic damage.[9] Furthermore, 5-FU offers chemoprevention for AKs and skin cancer, with reported decreased need for AK spot treatments and 75% decreased SCC following 5-FU treatment.[2,10] Topical 5-FU does have limitations: AK and SKC treatment requires multiple weeks of twice daily application, and patient compliance reportedly decreases with increasing treatment length.[11] Patients also describe the prolonged inflammatory reaction as uncomfortable and socially limiting.[8]

A recently proposed alternative to 5-FU monotherapy is 5-FU combined with vitamin D analog calcipotriene (5-FU/C). Initial reports suggest calcipotriene augments the 5-FU-mediated disruption of DNA synthesis via robust CD4+ T cell recruitment to damaged keratinocytes.[12,13] This synergy was first described in Cunningham et al (2017), a randomized clinical trial demonstrating 4 days of twice daily 5-FU/C resulted in 87.87% AK reduction in the treatment group (n = 64) versus 26.3% among controls (n = 65) 8 weeks posttreatment.[12] Post-hoc analysis of these data demonstrated 5-FU/C achieved greatest AK reductions on the face (forehead: 93.4%, temple: 94.8%, cheek: 90.2%), compared to scalp (83.4%) and forearm (69.7%).[14] The Oka et al trial (2025) examined average AK reduction after 6 days of twice daily 5-FU/C at 8 weeks (face: 95%, scalp: 82%, right upper extremity: 65%, left upper extremity: 68%).[13] Additional reports describe 5-FU/C for AKs treated with cryotherapy,[15] AKs located in the periocular area,[16] and AKs in immunosuppressed individuals.[17] Literature findings are summarized in Table I, demonstrating both efficacy and increased adoption of 5-FU/C for treatment of AKs.

Topical combined 5-FU/C may also prevent and treat skin cancer. Post-hoc analysis of Cunningham et al data by Rosenberg et al reported the 5-FU/C treatment group (n = 30) developed significantly fewer SCCs on face/scalp treatment fields compared to controls (n = 40) 3 years posttreatment.[18] A case series of 2 patients with xeroderma pigmentosum applying 5-FU/C every 3 to 6 months also described decreased skin cancer development from baseline with multiyear follow-up.[19] Recent studies showed 5-FU/C may effectively treat SKCs; a prospective clinical trial comparing 7 vs 14 days of twice daily 5-FU/C in SCCIS reported 83% and 88% of lesions were negative for residual tumor on pathology review 20+ days posttreatment, respectively.[21] A retrospective study of 209 SKCs (SCCIS and sBCC) among 163 patients demonstrated 91% clinical complete response rate overall after 5-10 days of twice daily 5-FU/C (mean follow-up: 15 months), with comparable response rates seen with adnexal extension (90%, n = 19) and immunosuppression (89%, n = 42).[20]

While promising, literature on 5-FU/C is currently limited to primarily single-institution studies with small sample sizes. Lack of consensus and high-quality data may limit clinicians' comfort treating AKs and SKCs with 5-FU/C. To address these limitations, members of the International Immunosuppression & Transplant Skin Cancer Collaborative (ITSCC) were surveyed and an expert panel convened to

Abbreviations used:

5-FU:	5-Fluorouracil
5-FU/C:	5-fluorouracil plus calcipotriene
AK:	actinic keratosis
ITSCC:	International Immunosuppression & Transplant Skin Cancer Collaborative
sBCC:	superficial basal cell carcinoma
SCCIS:	squamous cell carcinoma in situ
SKC:	superficial keratinocyte carcinoma

determine recommendations for 5-FU/C treatment of AKs and SKCs.

METHODS

This study was approved by Dartmouth-Hitchcock Medical Center institutional review board (STUDY02002837). The study was designed by members of ITSCC, a nonprofit organization of dermatologists, medical oncologists, transplant physicians, and researchers dedicated to advancing the care of patients at high-risk for skin cancer due to immunosuppression and/or organ transplantation. At the 2024 ITSCC Scientific Symposium, a workgroup identified treatment scenarios needing clarification for 5FU/C use and subsequently participated in a literature review and survey development. The literature review was performed on 5-FU/C treatment of AKs and SKCs (Table I). Search terms included "5-fluorouracil," "5-fluorouracil and calcipotriene," "5FU/C," "5-FU/C," "calcipotriene," "vitamin D analog," returning 10 original studies reporting treatment of AKs (6/10) and SKCs (2/10), and skin cancer prophylaxis (2/10). Based on the literature, the resulting survey was distributed electronically via REDCap to 118 ITSCC clinician members to assess 5-FU/C indications, treatment practices by lesion type and anatomic location, and uses in special populations. Survey participation was restricted to clinicians routinely prescribing 5-FU/C. Survey definitions were adapted from Actinic Damage and Skin Cancer Index (AD-SCI) and Actinic Keratosis Area and Severity Index (AKASI).[22]

Literature review results were shared with expert clinician participants, including the initial working group and additional ITSCC members with 5-FU/C experience and interest in contributing to an expert consensus recommendation. Preliminary consensus statements were developed by the working group based on survey responses and available literature data.

The expert consensus panel convened virtually in June 2025 and included 9 dermatologists and dermatologic surgeons with 5+ years post-training experience and/or extensive experience prescribing 5-FU/C. Consensus proceedings followed a modified Delphi method[23-25]; in the first round of the meeting, panelists independently voted "yes-agree" or "no-disagree" to each preliminary statement using an anonymous electronic survey, through which statement revisions could be suggested. Statements with <70% agreement were discussed in a second round and revised until consensus was reached.

RESULTS

Thirty-four ITSCC members participated in the initial survey (Supplementary Tables I-IV, available via Mendeley at https://data.mendeley.com/datasets/3xyf76fft9/1). Respondents were primarily surgical dermatologists (77%), had 5+ years of clinical experience (70%), worked in an academic setting (82%), and managed high risk skin cancer (82%). All reported experience prescribing 5-FU/C. While 94% prescribe 5-FU/C for moderate-to-severe AKs, only 53% and 20% prescribe 5-FU/C for SCCIS and sBCC, respectively, and 74% did not prescribe 5-FU/C to immunosuppressed individuals.

Expert panel consensus recommendations are outlined in Table II. Of 18 preliminary statements addressing 11 topics, 11 (61%) achieved >70% consensus on the first round of voting. Six remaining statements required further discussion and revision before achieving consensus. One statement was ultimately excluded due to insufficient evidence to make a recommendation.

The panel agreed that prescribing 5-FU/C as separate or compounded prescriptions should be determined by patient preference and cost. The recommended treatment for AKs with 5-FU/C was 4 to 5 days twice daily for face/neck, and 7 to 10 days twice daily for scalp, trunk, and extremities or for face/neck if initial regimen is unsuccessful. Clinical examination should inform how frequently 5-FU/C treatment is repeated; for extensive or rapidly recurring AKs, clinicians may recommend scheduled treatments every 3 to 6 months. 5-FU/C may be prescribed for sBCC, but data are limited, such that no recommendation regarding treatment duration was made and close clinical follow-up of these patients is advised. 5-FU/C treatment of SCCIS is gaining acceptance, with the panel recommending 7 to 10 days twice daily for face/neck and 10 to 14 days twice daily for scalp, trunk, and extremities. While no treatment modifications were recommended based on patient immune status, 5-FU/C use in immunosuppressed patients warrants close clinical follow-up to identify whether prolonged or more frequent treatment is needed. Actinic cheilitis may be treated with 4 to 5 days twice daily 5-FU/C; patient counseling regarding potentially severe local reaction

Table I. Literature review on use of topical 5-FU/C for the treatment of AKs, sBCC, and SCCIS

Study	Type	Treatment, *N*	Intervention	Results
Treatment of actinic keratoses				
Cunningham et al, 2017[12,†]	RCT	Tx: 5-FU/C, *n* = 64 Control: 5-FU + vaseline, *n* = 66	BID × 4d C: ointment, 0.005% 5-FU: cream, 5%	*Outcome: Reduction in AKs at 8 wk post-tx-* Face: 87.8% (tx, *n* = 45) vs 26.3% (control, *n* = 50) - Scalp: 76.4% (tx, *n* = 34) vs 5.7% (control, *n* = 34) - RUE: 68.8% (tx, *n* = 23) vs 9.6% (control, *n* = 26) - LUE: 79% (tx, *n* = 32) vs 16.3% (control, *n* = 31)
Moore et al, 2021[15]	Cohort, prosp.	Cryo only; *n* = 50 Cryo+5-FU, *n* = 50 Cryo+5-FU/C, *n* = 50 Cryo + calcipotriene, *n* = 25	BID × 5d (face) BID × 7d (non-face); q3 wk, eval. 101-200 & 201-300 d; C: foam, 0.005% 5-FU: cream, 1%	*Outcome: Reduction in AK compared to baseline-* 5-FU/C: significant at 101-200 and 201-300 d of treatment *Outcome = Reduction in AK compared to cryo-only-* 5-FU/C: significant at 101-200 & 201-300 d of treatment - Data not stratified by location
Diez et al, 2021[16]	Case series	Pt 1: 5-FU/C (OS), 5-FU (OD) Pt 2: 5-FU alone	BID × 4d C: ointment, 0.005% 5-FU: ointment, 5%	*Outcome: Clinical resolution of periocular AKs-* Improvement of AKs treated with 5-FU/C; pt 1 saw improved resolution with 5-FU/C compared to 5-FU monotherapy
Azin et al, 2022[14]	Post-hoc, RCT[12]	Tx: (5-FU/C, *n* = 54) Control: 5-FU + vaseline, *n* = 52	BID × 4d C: ointment, 0.005% 5-FU: cream, 5%	*Outcome: Reduction in AKs at 8 wk post-tx-* Forehead: 93.4% (tx, *n* = 37) vs 33.5% (control, *n* = 27) - Temples: 94.8% (tx, *n* = 18) vs 46.6% (control, *n* = 23) - Cheek: 90.2% (tx, *n* = 11) vs 44.3% (control, *n* = 19) - Scalp: 83.4% (tx, *n* = 25) vs 33.3% (control, *n* = 25) - Forearm: 69.7% (tx, *n* = 16) vs 27.2% (control, *n* = 17)
Junejo et al, 2023[17]	Survey	5-FU/C, *n* = 32* No control group *All immunosuppressed	Regimen & Rx type not reported	*Outcome: Patient opinion regarding 5-FU efficacy/experience-* 81% felt 5-FU/C was more effective than 5-FU - 87% preferred 5-FU/C to 5-FU - 47% felt local skin reaction was more severe in 5-FU/C - 53% felt local skin reaction was shorter in 5-FU/C

Continued

Table I. Cont'd

Study	Type	Treatment, *N*	Intervention	Results
Oka et al, 2025[13]	Clinical Trial	5-FU/C, *n* = 18 No control group	BID × 6d C: ointment, 0.005% 5-FU: cream, 5%	*Outcome: Reduction in AKs at 8 wk post-tx compared to baseline-* Face: 95% (*n* = 10) - Scalp: 82% (*n* = 13) - RUE: 65% (*n* = 7) - LUE: 68% (*n* = 8)
Skin cancer prevention/ treatment				
Rosenberg et al, 2019[18]	Post-hoc, RCT[12]	Tx: 5-FU/C (*n* = 41) Control: 5-FU/C + vaseline (*n* = 45)	BID × 4d C: ointment, 0.005% 5-FU: cream, 5%	*Outcome: SCC development at 3 years post-tx-* Face + Scalp: 7% (tx, *n* = 30) vs 28% (control, *n* = 40; *P* = .03) - No significant difference for face + scalp before 3 y, no significant difference for upper extremities
Kim et al, 2023[19]	Case series	Tx: 5-FU/C (*n* = 2)	BID × 4d, q3-6 mo Pt1, Compounded Rx* Pt2, C: unspecified 0.005% 5-FU: cream 5%	*Outcome: Skin cancer development post-tx in xeroderma pigmentosum-* "Near elimination" of new skin cancers in both patients
Loranger et al, 2025[20]	Cohort, retro.	Tx: 5-FU/C SCCIS; *n* = 179 sBCC; *n* = 30	BID × 5-10d Compounded Rx*	*Outcome: Clinical complete response, recurrence-free survival-* SCCIS: 92% CR (mean f/u 14.8 mo) and 95% 2-y RFS - sBCC: 83% CR (mean f/u 16.5 mo) and 84% 2-y RFS (not statistically different from SCCIS) - Local recurrence: 12% sBCC vs 2.4% of SCCIS (*P* = .03)
Patel et al, 2024[21]	Cohort, prosp.	Tx: 5-FU/C vs placebo cream SCCIS; *n* = 19 sBCC; *n* = 1, re-classified on path	BID × 7-14d vs placebo Compounded Rx*	*Outcome: Lesion resolution on pathology 20+ d post-tx-* SCCIS: 83.3% (7d tx, *n* = 6) and 87.5% (14d tx, *n* = 8) - sBCC: reclassified at path, not resolved after 7d tx

5-FU, 5-fluorouracil; *5-FU/C*, 5-fluorouracil/calcipotriene; *AK*, actinic keratosis; *BID*, twice daily; *C*, calcipotriene; *CR*, complete response; *cryo*, cryotherapy; *eval*, evaluation; *f/u*, follow-up; *KC*, keratinocyte carcinoma; *LUE*, left upper extremity; *OD*, right eye; *OS*, left eye; *prosp*, prospective; *Pt*, patient; *q*, every; *RCT*, randomized controlled trial; *retro*, retrospective; *RFS*, recurrence-free survival; *RUE*, right upper extremity; *rx*, prescription; *sBCC*, superficial basal cell carcinoma; *SCC*, squamous cell carcinoma; *SCCIS*, squamous cell carcinoma in situ; *tx*, treatment.
*Indicates 5-FU/C prescribed through compounding pharmacy, vs individual prescriptions to be combined at home by patient.
†Reports a secondary analysis of data from the Cunningham et al study[12].

Table II. Expert panel recommendations for use of topical 5-FU/C for the treatment of AKs and SKCs

Measure	Recommendation
All	
How should 5-FU/C be prescribed (compounded cream vs 2 separate prescriptions and patient combines at time of application)?*	Given no clear benefit regarding efficacy, the decision to prescribe 5-FU and calcipotriene individually and have patients combine at time of application or use a compounded product should be made based on cost and patient preference.
Actinic keratoses	
What 5-FU/C regimens are reasonable for treatment of AKs on the face & neck?†	The recommended treatment duration for AKs on the face and neck is BID × 4-5 d. If insufficient response of AKs on the face and neck after 4-5 d, a repeat treatment of BID × 7-10 d is reasonable.
What treatment regimens are reasonable for AKs on the scalp?*	The recommended treatment duration for AKs on the scalp is BID × 7-10 d.
What treatment regimens are reasonable for AKs on the trunk and extremities?*	The recommended treatment duration for AKs on the trunk and extremities is BID × 7-10 d.
When treating AKs with 5-FU/C how often should this be repeated?†	Repeat courses of 5-FU/C should be recommended based on clinical examination. In high-risk, rapidly recurring cases with extensive actinic skin damage, scheduled treatments every 3-6 mo is useful for treatment and chemoprevention.
Superficial basal cell carcinoma	
Can 5-FU/C be used for treatment of sBCC?*	5-FU/C is rarely used for the treatment of sBCC, but can be considered in patients who cannot be managed surgically or with other currently FDA-approved treatments.
What treatment regimens are reasonable for sBCCs?†	There is not enough data to recommend a specific treatment duration for sBCC. If a provider chooses to treat sBCC with 5-FU/C, close clinical follow-up is recommended.
Squamous cell carcinoma in situ	
Can 5-FU/C be used for treatment of SCCIS?*	5-FU/C is gaining acceptance for the treatment of SCCIS and can be considered in patients who cannot be managed surgically or with other currently FDA-approved treatments.
What treatment regimens are reasonable for SCCIS?*	The recommended treatment duration for SCCIS on the face and neck is BID × 7-10 d. The recommended treatment duration for SCCIS on the scalp, trunk, and extremities is BID × 10-14 d.
Special considerations	
What modifications to treatment could be considered in immunosuppressed patients?†	Initial treatment protocols for immunosuppressed and immunocompetent patients should be the same. Immunosuppressed patients merit close follow-up as they may require prolonged or more frequent treatment courses.
Is it reasonable to treat actinic cheilitis with 5-FU/C?†	Based on expert consensus, it is reasonable to treat actinic cheilitis with 5-FU/C for a duration of BID × 4-5 d with appropriate patient counseling regarding possibility of a severe reaction.

5-FU/C, 5-fluorouracil/calcipotriene; *AK*, actinic keratosis; *BID*, twice daily; *sBCC*, superficial basal cell carcinoma; *SCCIS*, squamous cell carcinoma in situ.

*Reached ≥70% consensus in first round of voting.

†Required panel discussion and statement revision to achieve consensus.

is advised. Recommendations for 5-FU/C use in genital and periocular regions did not reach consensus given limited evidence and experience.

DISCUSSION

5-FU/C is gaining acceptance as topical chemotherapy for treatment of AKs and SKCs; however, use in the community may be hindered by limited available data and therapy novelty. Hesitations surrounding 5-FU/C include theoretical risk of more severe inflammatory reactions compared to 5-FU monotherapy given the relatively more robust and rapid CD4+ T cell immune response, with resulting inflammation typically peaking 10 to 11 days after application.[12,13] This may present as localized edema, erythema, discomfort, and erosions. Potential adverse effects include hypersensitivity reaction and superinfection, as well as difficulty eating when treating actinic cheilitis. While patient-reported perspectives suggest comparable reactions from 5-FU/C and 5-FU monotherapy, recommendations regarding 5-FU/C indications and prescription practices are lacking.[16,17] Our expert dermatologist panel convened to address these gaps and potential hesitations by creating consensus recommendations based on available literature and clinical experience.

Consensus on 5-FU/C treatment of AKs was more quickly attained than for other indications, likely because AK treatment comprises most of the published literature and expert experience with 5-FU/C. Recommendations regarding AK treatment duration achieved consensus on the first round of the meeting, and further discussion yielded the recommendation that severe/extensive actinic damage on face/neck may warrant extension if response is insufficient. These recommendations reflect the Cunningham et al and Azin et al clinical trial findings that demonstrated greater efficacy treating AKs on the face vs other sites, suggesting other locations may require longer treatment.[12,14] While swelling and erythema are expected, their absence may represent an insufficient response, possibly meriting treatment extension until the expected inflammatory reaction is obtained. Persistently non-responsive lesions may merit biopsy, and caution is advised when treating transected lesions or those located on terminal hair-bearing skin; providers should use their best clinical judgement when considering topical therapy.

A less common but growing indication for 5-FU/C is SCCIS. Approximately half of survey participants reported treating SCCIS with 5-FU/C, possibly due to a lack of high-quality data in this area; only 2/10 original 5-FU/C studies treated SCCIS, including a retrospective, dual-center cohort study (n = 209) and a small clinical trial (n = 14).[20,21] Though limited, evidence published thus far is promising; Loranger et al reported 92% complete clinical response rate for SCCIS with just 2% local recurrence rate (mean follow-up: 14.8 months) and 95% 2-year recurrence-free survival.[20] Patel et al described 83% and 88% resolution on pathology for SCCIS treated 7 and 14 days with twice daily 5-FU/C, respectively, at 20+ days posttreatment.[21] Other studies report 5-FU/C as chemoprophylaxis: Rosenberg et al reported significantly fewer SCCs on face/scalp 3 years posttreatment with 5-FU/C vs 5-FU monotherapy, while Kim et al saw decreased skin cancer development with quarterly 5-FU/C application in 2 patients with xeroderma pigmentosum.[18,19] Larger, prospective, randomized clinical trials are needed. At the time of this study, 6 clinical trials on 5-FU/C were recruiting or completed: 4 treating AKs and 2 treating skin cancer.[26]

Regarding 5-FU/C treatment of sBCC, the panel ultimately felt there was insufficient evidence to make a recommendation. Only 20% of survey participants treat sBCC with 5-FU/C, likely because few studies included BCC. Loranger et al reported 83% complete clinical response (mean follow-up: 16.5 months) and 84% 2-year recurrence-free survival among 30 sBCCs. While promising, interpretability is limited by small sample size.[20] Some studies incidentally reported on BCCs; Patel et al excluded a tumor from final analysis after reclassification as BCC on pathology review, noting lesion persistence despite 7 days of twice-daily 5-FU/C.[21] Rosenberg et al reported no significant decrease in BCC development up to 3 years after 4 days of twice daily 5-FU/C vs 5-FU monotherapy, and the BCC tumor microenvironment demonstrated decreased T cell response than was seen in AK/SCC, possibly reflecting differential mutational burden between lesion types.[18]

Similarly, no specific recommendation was made regarding formulation. Clinicians can prescribe 5-FU/C via compounding pharmacy (5% 5-FU, 0.005% calcipotriene) or separate 5-FU and calcipotriene prescriptions that patients combine 1:1 before application, effectively halving the doses (2.5% 5-FU, 0.0025% calcipotriene). Experts noted at-home combination may yield variable results due to inconsistencies in mixing/application, but may be more affordable as the compounded version is generally not covered by insurance. Given the lack of evidence to indicate superiority for either approach, the panel recommended that patient preference and cost guide this decision. Data comparing efficacy and outcomes of different prescription vehicles, such as ointment, cream, and foam, are also lacking (Table I). Vehicle choice may impact shelf life, which also has not been studied and likely impacts treatment efficacy. Anecdotally, experts reported identifying "non-responder" patients who had used expired

5-FU/C cream, highlighting prescription expiration as a potential confounder in studies examining treatment efficacy. Data regarding 5-FU/C treatment repetition in patients with severe AKs or at high-risk for skin cancer is also sparse; Kim et al described 5-FU/C use 3-4 times annually in xeroderma pigmentosum patients, and Moore et al described cyclical application of 5-FU/C after cryotherapy.[15,19] No studies reported on 5-FU/C treatment repetition, though our experts report this is often required in severe cases. Future studies are needed to clarify the impact of using compounded products vs individual prescriptions, as well as the impact of patients mixing creams vs applying separately and sequentially.

Limited data exist on outcomes in immunosuppressed patients using 5-FU/C. One study described comparable complete clinical response rate in immunosuppressed patients compared to the cohort overall (89% vs 91%, respectively; average follow-up = 15 months), while a survey of immunosuppressed patients found most patients (26/32, 81%) felt 5-FU/C was more effective than 5-FU monotherapy in AK clearance.[17,20] Cunningham et al excluded immunosuppressed individuals, though one 5-FU/C cohort participant was later diagnosed with an immunosuppressive condition and ultimately excluded from analysis; this patient saw just 19% AK reduction 8 weeks posttreatment (face) compared to the average 87.8% reduction.[12] Though our expert panel felt their experience and current evidence did not support regimen modification in immunosuppressed patients, more data are needed.

Finally, few studies report 5-FU/C use in sensitive anatomic locations. While multiple providers reported treating actinic cheilitis with 5-FU/C, no literature addresses this to date. Periocular use is also infrequently reported; while 1 case series of 2 patients using 5-FU/C for periocular AKs resulted in subjective clinical improvement in both cases, a retrospective series of 14 cases using 5-FU alone periocularly reported mild keratopathy and chemosis in 2 participants.[16,27] As such, the panel declined to make a recommendation on periocular application of 5-FU/C. As no studies report 5-FU/C use on the genitals, the panel declined to recommend use on these sensitive areas.

LIMITATIONS

This study is limited by the small sample size of survey and panel participants and limited available literature on 5-FU/C. These recommendations are not comprehensive, but rather a targeted set of recommendations for 5-FU/C treatment of AKs and SKCs by anatomical location.

CONCLUSIONS

We herein summarize the recommendations made by our expert consensus panel regarding 5-FU/C use for AKs and SKCs. 5-FU/C is an affordable and effective therapy, especially for treatment of AKs and SCCIS, that helps prevent development of invasive skin cancers and condenses the patient-reported lengthy and uncomfortable regimen attributed to 5-FU monotherapy. Standardizing treatment duration and indication of 5-FU/C will allow for improved interpretation between studies and more optimal treatment of AK and SKC lesions.

Conflicts of interest

None disclosed.

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