Table I. Patient demographics

Variable	Result (N = 20)
Age, average (range), y	31.11 (21-40)
Sex, No.	
Male	15
Female	5
Nails involved, No.	89
Thumb, % (No.)	40.45 (36)
Index finger, % (No.)	37.08 (33)
Middle finger, % (No.)	17.98 (16)
Ring finger, % (No.)	2.24 (2)
Little finger, % (No.)	2.24 (2)
Nails treated per patient, No.	4.45
NAPSI score, mean (range)*	
0 weeks (baseline)	3.70 (10-30)
6 weeks	1.83 (4-20)
12 weeks (post-treatment)	0.67 (0-20)
Dose of methotrexate per patient, average (range) mg	135 (60-300)
Duration of psoriasis before treatment, range	1-15 years
Previous treatment tried	Topical corticosteroids, calcipotriol, tacrolimus, tazarotene
Concomitant treatment	Oral ibuprofen for pain, to be taken on an as-needed basis

NAPSI, Nail Psoriasis Severity Index.
*Follow up mean NAPSI scores were based on intention-to-treat analysis, using the baseline scores of the patients who were lost to follow-up.

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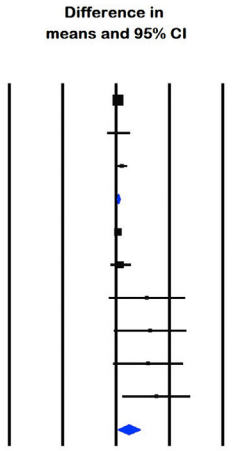
Chemoprevention of keratinocyte carcinoma and actinic keratosis in solid-organ transplant recipients: Systematic review and meta-analyses

To the Editor: Skin cancers account for 40% of malignancies in solid-organ transplant recipients (SOTRs), who have an 80-fold increased risk of squamous cell carcinoma (SCC) and a 16-fold increased risk of basal cell carcinoma (BCC). Systemic chemoprevention is one method to mitigate this amplified risk. Acitretin, for instance, has been used to prevent keratinocyte carcinomas (KC) and actinic keratoses (AK) in SOTRs since 1995,[1] but its adverse effects include mucositis, liver and lipid abnormalities, and teratogenicity.[2] Nicotinamide, an amide form of vitamin B_3, is a newer chemoprophylaxis with fewer adverse effects.[3] Here we report results of a pairwise and network meta-analyses to summarize the current evidence regarding chemoprevention.

We selected studies that analyzed the efficacy of systemic chemoprevention to prevent KC/AK in patients who are SOTRs or have a history of 2 or more KCs, or both. We limited our search to placebo-controlled, randomized control trials (RCTs) that reported the number of new KC/AK in both arms. Two authors (L.Y.T., S.Y.C.T.) independently conducted the literature search, screened titles and abstracts for eligibility, and extracted data. Statistical synthesis was performed with RevMan 5.3 software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

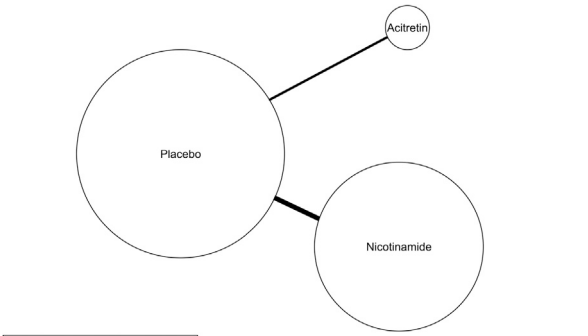
After the literature search, 6 RCTs with 734 patients were included in the quantitative synthesis (Appendix A, available via Mendeley at https://doi.org/10.17632/m6z2fzkkxn.2). Of the 6 RCTs, 3 studies with 580 patients (range, 17-192 patients) compared nicotinamide to placebo, and 3 studies with 154 patients (range, 19-35 patients) compared acitretin to placebo. Pairwise meta-analysis of all 6 RCTs using a random-effects model demonstrated a significant risk reduction with chemoprevention (Fig 1). The overall mean difference was 0.855 (95% confidence interval, 0.365-1.345; $P < .001$). In addition, acitretin and nicotinamide were both efficacious, with a combined mean difference of

Group by Treatment	Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Acitretin	Bavinck 2005	0.68	0.27	0.07	0.16	1.20	2.55	0.01
Acitretin	George 2002	0.83	1.85	3.43	-2.80	4.46	0.45	0.66
Acitretin	Kadakia 2012	1.90	0.84	0.71	0.25	3.55	2.26	0.02
Acitretin		0.79	0.25	0.06	0.30	1.29	3.14	0.00
Nicotinamide	Chen 2015	0.65	0.30	0.09	0.06	1.24	2.16	0.03
Nicotinamide	Chen 2016	1.50	1.63	2.67	-1.70	4.70	0.92	0.36
Nicotinamide	D Surjana, 2012 (a1)	10.10	6.36	40.39	-2.36	22.56	1.59	0.11
Nicotinamide	D Surjana, 2012 (b1)	11.20	6.00	36.05	-0.57	22.97	1.87	0.06
Nicotinamide	D Surjana, 2012 (a2)	10.50	5.77	33.35	-0.82	21.82	1.82	0.07
Nicotinamide	D Surjana, 2012 (b2)	13.20	5.62	31.59	2.18	24.22	2.35	0.02
Nicotinamide		4.24	1.85	3.43	0.61	7.87	2.29	0.02



Heterogeneity: I^2=47.22%, Tau^2=0.4629, p=0.00561

Fig 1. Forest plot of the pairwise meta-analysis of randomized controlled trials. The *squares* indicate the mean difference and are proportional to the weights used in the meta-analysis. The *horizontal lines* represent the 95% confidence interval (*CI*). The *diamond* indicates the weighted mean difference, and the *lateral tips* of the diamond indicate the associated 95% CI.



Acitretin		
-1.19 (-4.12; 1.74)	Nicotinamide	
1.14 (-0.79; 3.08)	2.33 (0.13; 4.53)	Placebo

Fig 2. Network graph and league table of the network meta-analysis. Mean differences and 95% confidence intervals are calculated using a random-effects model. A mean difference >1 means the top-left treatment is better.

0.792 (95% confidence interval, 0.298-1.286; $P = .00168$) for acitretin and a combined mean difference of 4.239 (95% confidence interval, 0.611-7.866; $P = .0220$) for nicotinamide. A network meta-analysis comparing nicotinamide and acitretin found no significant difference between the 2 treatments (Fig 2, Appendix B).

This meta-analysis does not address the optimal dosages of the drugs or the frequency of adverse effects. In addition, owing to the limited numbers of eligible RCTs, we are unable to investigate how chemoprevention is influenced by the duration or type of transplantation, duration of systemic chemoprevention, or existing immunosuppressive regimens. Moving forward, topical chemoprevention may be a suitable alternative to systemic chemoprophylaxis in SOTRs. Notably, large RCTs have evaluated topical chemoprevention for actinic keratosis. For instance, the Veterans Affairs Keratinocyte Carcinoma Chemoprevention trial found that topical 5% 5-fluorouracil cream resulted in a 49% relative risk reduction in the number of AK after 6 months and reduced the risk of SCC requiring surgery by 75% after 1 year but did not lower the risk of BCC.[4,5]

To our knowledge, this is the first meta-analysis that statistically integrates the current evidence regarding chemoprevention of KC/AK. This study demonstrates that systemic chemoprevention with nicotinamide or acitretin is effective in lowering the risk of KC/AK. Yet, even with the advent of better chemoprevention, regular physician surveillance and sun protection are still key basic strategies that should be practiced by all SOTRs.

Louis Y. Tee, MD, PhD,[a] Rehena Sultana, MS,[b] Steve Y. C. Tam, BS,[c] and Choon Chiat Oh, MD[a]

From the Department of Dermatology, Singapore General Hospital,[a] the Centre for Quantitative Medicine, Duke- National University of Singapore (NUS) Medical School, Singapore,[b] and Singapore General Hospital Library, Singapore Health System, Singapore, Singapore.[c]

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Correspondence to: Choon Chiat Oh, MD, Singapore General Hospital, Department of Dermatology, Academia Level 4, 20 College Rd, Singapore 169856

E-mail: oh.choon.chiat@singhealth.com.sg

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$CD30^+$ leukemic cutaneous T-cell lymphoma

To the Editor: CD30 is a tumor necrosis factor receptor involved in regulating apoptosis and proliferation of $CD30^+$ tumor cells.[1] $CD30^+$ T cells are primarily expressed in conditions such as primary cutaneous $CD30^+$ T-cell lymphoproliferative disorders and some peripheral T-cell lymphomas, and they can potentially be expressed in any type of cutaneous T-cell lymphoma (CTCL).[2-4] However, CD30 expansion on the leukemic cells of patients with CTCL or Sézary syndrome is rare, and little is known regarding the natural history and prognosis of patients with leukemic CTCL expressing this cell type.[2,3,5]

After approval by an institutional review board, we identified all patients with a clinical diagnosis of leukemic CTCL or Sézary syndrome and reviewed the medical records of those exhibiting CD30 expression on the skin, in lymph nodes, or in blood from January 1, 1994, to August 31, 2017. Among 44 patients diagnosed with leukemic CTCL, 6 (13.6%) were found to have some degree of CD30 expression on the leukemic cells. Only 3 of the 6 patients had complete records available for review.

Patient 1, a 57-year-old white man, presented with a 1-year history of a generalized folliculocentric eruption unresponsive to topical steroids. Blood flow cytometry (FC) showed an abnormal population of T cells (10% of all events), phenotypically $CD2^+$, $CD3^+$, $CD4^+$, $CD8^-$, $CD5^+$, CD7 partial, CD25 dim/negative, $CD26^-$, CD30 partial (Fig 1, *A-D*). The $CD4^{hi}$ (nonmalignant, red) cells, which are $CD7^+$ (Fig 1, *B*) and $CD26^+$ (Fig 1, *C*), are $CD30^-$ or very dim (Fig 1, *D*) relative to the CD4 dim (blue) malignant population. The patient was diagnosed with mycosis fungoides with B1 involvement and treated with extracorporeal photopheresis (ECP) and narrowband ultraviolet B, with significant improvement. His disease has continued to remain well controlled 5 years after the initial diagnosis.

Patient 2, a 55-year-old man, had Sézary cells on peripheral smear and blood FC showing an abnormal population of T cells (83% of all events), phenotypically $CD2^+$, $CD3^+$, $CD4^-$, $CD8^-$, $CD5^+$, CD7 partial, $CD25^-$, $CD26^-$, TCR$\alpha\beta^+$, and a small portion of $CD30^+$ cells (Fig 1, *E*). He was diagnosed with stage IV Sézary syndrome and despite treatment with vorinostat and ECP, he died 6 years after presentation.

Patient 3, a 77-year-old white man with blood FC showing an abnormal population of T cells (approximately 14% of all events), phenotypically CD2 dim, $CD3^+$, $CD4^+$, $CD8^-$, $CD5^+$, $CD7^+$, CD25 dim, $CD26^-$ (16%), and a partial portion of $CD30^+$ cells (Fig 1, *F*). He was diagnosed with mycosis fungoides and received several treatments including ECP, bexarotene, and vorinostat. After several years of treatment, the patient self-discontinued therapy and died 7 years after presentation.

Because of challenges in the treatment of leukemic CTCL, it is important to understand its phenotypic variants and their implications for prognosis and treatment response. There has been little to no information on the expression of $CD30^+$ T cells in the blood of patients with leukemic CTCL. To our knowledge, CD30 is not routinely assessed on blood FC. Recent developments in the treatment of CTCL include antibody-based immunotherapies, including anti-CD30 brentuximab vedotin, currently approved for treatment of $CD30^+$ Hodgkin lymphoma, $CD30^+$ lymphoproliferative disorders, and CD30-expressing mycosis fungoides.[5,6] However, the nature of patients treated with brentuximab vedotin who have circulating $CD30^+$ cells is not yet clear.[5] Therefore, a better understanding of the role of leukemic CD30 positivity in the history, prognosis, and association with other prognostic factors and its significance in the development of more specific antineoplastic therapies may be beneficial to the treatment of patients with leukemic CTCL.