

SUPPLEMENTARY DATA

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A regimen to minimize pain during blue light photodynamic therapy of actinic keratoses:
Bilaterally controlled, randomized trial of simultaneous versus conventional illumination

Urvashi Kaw, MD¹; Muneeb Ilyas¹, DO; Taylor Bullock, BS¹; Lisa Rittwage, BSN RN¹; Margo Riha, BSN RN¹; Allison Vidimos, MD MPH¹; Bo Hu, PhD²; Christine B. Warren, MD MS¹;
Edward V. Maytin, MD PhD^{1, 3}

¹ Departments of Dermatology, and ²Quantitative Health Sciences, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195

³ Corresponding author: Edward V. Maytin, MD PhD, Desk A60, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195 E-mail: maytine@ccf.org

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SUPPLEMENTARY TABLE 1.

Patient demographics, bilateral AK lesion counts at baseline (Visit 1), and absolute and relative changes in AK lesion counts at 3 months after treatment (Visit 2) on the side receiving either Simultaneous (S) or Conventional (C) PDT.

Demographic information			Number of AK Lesions on the Face								Number of AK Lesions on the Scalp								
Patient ID	Sex	Age (Yr)	Visit 1		Visit 2		Absol Decr ^[c]		Rel Decr ^[d] (%)		Visit 1		Visit 2		Absol Decr		Rel Decr (%)		
			S ^[a]	C ^[b]	S	C	S	C	S	C	S	C	S	C	S	C	S	C	
(1)	30b-18	F	73	14	10	5	2	9	8	64	80	0	0	0	0	-	-	-	-
(2)	30b-17	M	72	24	26	11	14	13	12	54	46	14	20	10	10	4	10	29	50
(3)	30-04	M	87	27	10	6	5	21	5	78	50	44	18	13	9	31	9	70	50
(4)	30-03	M	70	56	49	30	24	26	25	46	51	0	0	0	0	--	-	-	-
(5)	30b-16	M	71	29	17	17	7	12	10	41	59	0	0	0	0	--	-	-	-
(6)	30-05	M	73	21	16	14	7	7	9	33	56	11	9	7	5	4	4	36	44
(7)	30b-29	M	88	32	38	9	16	23	22	72	58	59	64	25	41	34	23	58	36
(8)	45b-19	M	73	27	28	15	10	12	18	44	64	13	12	5	10	8	2	62	17
(9)	45-06	M	58	9	10	1	1	8	9	89	90	16	22	11	11	5	11	31	50
(10)	45b-20	M	74	23	16	8	10	15	6	65	38	59	66	38	45	21	21	36	32
(11)	45-10	M	61	13	7	1	3	12	4	92	57	13	13	8	8	5	5	38	38
(12)	45-07	M	72	7	16	6	2	1	14	14	88	0	0	0	0	--	-	-	-
(13)	45-08	M	58	15	13	10	9	5	4	33	31	24	10	18	6	6	4	25	40
(14)	45b-21	M	66	26	23	14	14	12	9	46	7	51	46	28	28	23	18	45	64
(15)	45b-23	M	69	19	17	1	1	18	16	95	94	0	0	0	0	--	-	-	-
(16)	60-12	M	74	13	10	6	5	7	5	54	50	10	10	4	5	6	5	60	50
(17)	60-15	M	76	20	11	5	1	4	10	44	91	11	7	6	5	5	2	45	29
(18)	60-14	M	69	7	2	3	2	4	0	57	0	12	13	4	3	8	10	67	77
(19)	60-13	M	72	17	27	14	14	3	13	18	48	0	0	0	0	--	-	-	-
(20)	60-11	M	70	7	13	3	1	4	12	57	92	13	13	8	8	5	5	38	38
(21)	60b-24	M	63	16	17	2	7	14	10	88	59	25	31	20	24	5	7	20	23
(22)	60b-25	M	66	9	18	4	6	5	12	56	67	27	22	16	15	11	7	41	32
(23)	60b-26	F	50	53	24	4	4	25	20	86	83	0	0	0	0	--	-	-	-

FOOTNOTES:

- [a] Side of the body that received Simultaneous incubation/illumination (S).
- [b] Side of the body that received Conventional incubation (1 h) followed by illumination (C).
- [c] Absolute decrease in AK lesion counts.
- [d] Relative decrease in AK lesion counts with respect to baseline (%).

SUPPLEMENTARY TABLE 2.

Pain scores reported during simultaneous *versus* conventional PDT illumination.

<i>Patient ID</i>	<i>Simultaneous PDT Side</i>						<i>Conventional PDT side</i>			
	Time during illumination (min)						Time during illumination (min)			
	10'	20'	30'	40'	50'	<i>Mean</i>	5'	10'	15'	<i>Mean</i>
(1) 30b-18	0	0	0	-	-	0.0	5	5	4	4.7
(2) 30b-17	0	0	0	-	-	0.0	2	1	0	1.0
(3) 30-04	2	2	2	-	-	2.0	10	7	5	7.3
(4) 30-03	3	5	6	-	-	4.7	10	5	6	7.0
(5) 30b-16	0	1	1	-	-	0.7	4	4	4	4.0
(6) 30-05	1	1	1	-	-	1.0	5	3	1	3.0
(7) 30b-29	0	0	0	-	-	0.0	3	3	3	3.0
(8) 45b-19	0	0	0	0	-	0.0	8	3	0	3.7
(9) 45-06	1	0	0	0	-	0.3	4	3	2	3.0
(10) 45b-20	1	1	1	1	-	1.0	3	3	2	2.7
(11) 45-10	0	0	0	0	-	0.0	2	2	1	1.7
(12) 45-07	0	0	0	1	-	0.3	4	4	3	3.7
(13) 45-08	0	0	0	0	-	0.0	4	5	4	4.3
(14) 45b-21	1	1	0	0	-	0.5	5	5	5	5.0
(15) 45b-23	0	0	0	0	-	0.0	1	1	2	1.3
(16) 60-12	0	0	0	0	0	0.0	1	1	0	0.7
(17) 60-15	1	0	1	1	1	0.8	8	6	5	6.3
(18) 60-14	0	0	0	0	1	0.2	5	4	4	4.3
(19) 60-13	0	0	0	0	0	0.0	1	1	1	1.0
(20) 60-11	0	0	0	0	0	0.0	4	4	3	3.7
(21) 60b-24	0	1	1	1	1	0.8	8	7	5	6.7
(22) 60b-25	0	0	0	0	0	0.0	0	1	0	0.3
(23) 60b-26	0	0	0	0	0	0.0	2	4	5	3.7

FOOTNOTES:

- Pain values shown here were reported every 5 to 10 minutes on a 0-to-10 visual-analog scale (VAS). The highest value of 10 was defined as unbearable pain.
- Statistical comparison of VAS pain scores between simultaneous and conventional regimens showed the following: The mean score on Side A was **0.52** (95% CI=[0, 1.09]), and on Side B was **3.57** (95% CI=[2.97, 4.16]). The two sides were significantly different, with a p-value <0.001.

SUPPLEMENTARY TABLE 3.

Inflammatory responses reported during the first 4 days after photodynamic therapy:

Comparison between the sides receiving Simultaneous PDT or Conventional PDT

Symptom ^[c]	DAY 1	DAY 2	DAY 3	DAY 4
	Simult ^[a] Conven^[b]	Simult Conven	Simult Conven	Simult Conven
(A) Bleeding	0 0	17 0	13 4	17 13
(B) Blisters	13 13	4 9	17 13	4 9
(C) Burning	65 65	52 52	35 35	26 26
(D) Crusting	9 4	9 17	30 26	35 35
(E) Itching	43 43	74 74	70 65	65 65
(F) Open sores	0 0	9 9	9 9	4 4
(G) Peeling	4 0	4 9	22 26	48 52
(H) Redness	91 91	100 100	91 87	83 74
(I) Stinging	65 65	70 70	39 39	35 35
(J) Swelling	26 22	26 26	9 13	0 0
(K) Pain Score ^[d]				
Mean:	3.0 2.9	2.5 2.4	1.6 1.5	1.0 1.0
SEM:	± 0.64 ± 0.62	± 0.53 ± 0.51	± 0.33 ± 0.31	± 0.22 ± 0.21

FOOTNOTES:

^[a] *Simult* refers to the side of the body that received *Simultaneous* ALA incubation and blue light illumination (Side A).

^[b] *Conven* refers to the side of the body that received the *Conventional* PDT regimen with a 1 hr ALA preincubation prior to blue light illumination (Side B).

^[c] Each value in the table is a percentage of patients who reported the particular symptom (**A** to **J**).

^[d] Average pain score (0-10 visual-analog scale) reported by the 23 patients, on Side A and Side B.

SUPPLEMENTARY TABLE 4.

Results of an ancillary trial to evaluate the effect of ALA and ambient light upon facial actinic keratoses (AK) in nine patients.

Pt #	Study ID	Sex	Age (Yr)	Month*	<i>Number of AK Lesions on the Face</i>			
					Absolute Counts		Rel. Change (%)	
					Visit 1	Visit 2		(Diff)
1	A30	M	73	Jun	17	16	-1	- 5.9%
2	A32	F	68	Feb	49	45	-4	- 8.2%
3	A37	M	70	Feb	123	109	-14	- 11.4%
4	A36	M	73	Feb	19	15	-4	- 21.1%
5	A35	F	69	Feb	33	23	-10	- 30.3%
6	A34	M	74	Feb	6	4	-2	- 33.3%
7	A33	M	70	Mar	12	8	-4	- 33.3%
8	A38	M	81	Apr	27	17	-10	- 37.0%
9	A39 **	M	76	Apr	19	38	19	+100.0%

FOOTNOTES:

Nine subjects with AK on the face were recruited for this small ancillary study to examine the possible treatment effect that ambient light may exert upon AK lesions after ALA application, in the absence of any blue light exposure. At Visit 1 the AK lesions were marked, photographed, and counted. Topical ALA was applied to the face but no blue light illumination was performed. Instead, patients were sent home with a hat after instructing them to avoid sunlight and bright indoor lights for 48 h. These are the same instructions typically given to PDT patients in a real world setting. At a second study visit three months later (Visit 2), AK lesions were again evaluated by photography and clinical examination. Most patients participated in this study during the winter/spring of 2018 (February-April).

As shown in the table, all but one patient had a decline in the AK lesion count between Visit 1 and Visit 2. For the eight patients who showed a reduction in their lesion counts, the average decrease in the number of AK (mean ± SD) was 22.6 ± 12.6%. Overall, the mean change in AK lesion count for all nine patients was -8.9%.

* Time of year when the ALA was applied