H.8 Phototherapy

H.8.1 Narrow-band UVB vs broad-band UVB (between-patient randomisation)

<table>
<tr><th>Reference</th><th>Study type</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr>
<td>S. M. Kirke, S. Lowder, J. J. Lloyd, B. L. Diffey, J. N. Matthews, and P. M. Farr. A randomized comparison of selective broadband UVB and narrowband UVB in the treatment of</td>
<td>RCT

Single-centre (phototherapy unit), UK

Recruited May 2003 – Nov 2004

• Randomised (permuted blocks within strata)
• No explicit ‘washout’ or run-in period (but see</td>
<td>Total N: 100

Drop-outs (don’t complete the study):

N=6 drop-outs in TL01 arm: 3 failed to attend for treatments and 3 withdrew because of side effects</td>
<td>Inclusion criteria: Plaque psoriasis; ≥18 years of age,

Exclusion criteria: received phototherapy or systemic agents for psoriasis in the preceding 3 months

Note: allocation stratified by:
• plaque size (small <3 cm diameter) or large (>3 cm diameter)
• involvement of skin around or below the knees
• skin type (I/II or III/IV)

<table>
<tr><th>Mean baseline</th><th>TL01 (n=50)</th><th>UV6 (n=50)</th></tr>
<tr><td>Mean age –</td><td>42 (19-</td><td>39 (17-</td></tr>
</table>
</td>
<td>N=50

Selective broadband UVB (UV6 – little emission below 290 nm), three-times weekly

Administered using whole-body exposure units fitted with 40 fluorescent lamps

Dose determined by</td>
<td>N=50

Narrow-band UVB (TL-01), three-times weekly

Administered using whole-body exposure units fitted with 40 fluorescent lamps

Dose determined by minimal erythematic</td>
<td>6 months (plus unclear Tx duration – at least 5.5 weeks)</td>
<td>1° outcome: median number of treatments to clear

Clearance = no residual psoriasis or psoriasis only remaining in areas shaded from UV exposure, e.g., flexures

2° and</td>
<td>None stated</td>
</tr>
</table>

psoriasis. *J.Invest.Dermatol.* 127 (7):1641-1646, 2007. Ref ID: KIRKE2007	exclusion criteria) • Observer blinded • Allocation concealment using opaque, sealed, sequentially number envelopes • Sample size calculation based on 80% power to detect change in 1° outcome of 25% at 5% significance • ITT analysis – assumptions not stated • N=4 drop-outs/withdrawals due to AEs (n=3 TL01, N=1 UV6)	N=9 drop-outs in UV6 arm: 8 failed to attend for treatments and 1 withdrew because of side effects	<table><tr><td>years (range)</td><td>76)</td><td>77)</td></tr><tr><td>Gender M/F</td><td>50%/50%</td><td>40%/60%</td></tr><tr><td>Mean baseline PASI (range)</td><td>7.5 (2.1-27.9)</td><td>6.1 (2.7-21.7)</td></tr></table> The 2 groups were similar for baseline characteristics	minimal erythematic dose (MED) measurement by testing on the forearm and judged visually 24 h after irradiation. --- **BOTH ARMS: stepped Tx strategy** Initial dose 70% MED, increased 40% after alternate treatments, decreasing stepwise to 5% by the 18th treatment (dose increments postponed if erythema developed)	dose (MED) measurement by testing on the forearm and judged visually 24 h after irradiation. --- **BOTH ARMS:** Emollients only permitted Planned withdrawal permitted after 16 treatments; treatment was continued until psoriasis cleared or no further improvement was made		**other outcomes:** clearance of psoriasis, PASI scores for non-clearing participants, patients remaining clear, adverse events	

Effect Size

Outcomes (ITT population - included all patients)

Outcome	**TL01** **(N=50; ITT)**	**UV6** **(N=50; ITT)**	**Ratio of medians (95% CI)**	**p-value**
1° outcome: number of exposures for clearance (median adjusted for stratification variables; based on Weibull distribution)	28.4	30.4	0.93 (0.80-1.09)	0.39
Outcome	**TL01** **(N=50; ITT)**	**UV6** **(N=50; ITT)**	**Odds ratio (adjusted for stratification factors; 95% CI)**	**p-value**
Clearance of psoriasis – time of assessment not reported	28	20	2.00 (0.87-4.62)	0.10

Effect of stratifying factors:

Comparison	**Odds of clearance**	**95% CI and p-value**

Plaque size: large relative to small	0.71	0.30, 1.68 P=0.43
Skin type: III/IV relative to I/II	3.22	1.40, 7.43 P=0.006
Involvement of skin around or below knees: No relative to yes	1.11	0.41, 3.02 P=0.84

Mean PASI scores in non-clearing patients

	Mean TL-01 (*n*)	**Mean UV6 (*n*)**	**Difference and 95% CI**	***P*-value**
Score at baseline				
All patients failing to clear	7.4 (22)	6.8 (30)	0.6 (-2.6, 3.9)	0.69
Patients failing to clear who made a planned exit from the trial	8.3 (16)	5.8 (21)	2.5 (-1.4, 6.4)	0.20
Last PASI available				
All patients failing to clear	3.8 (22)	3.9 (30)	0.0 (-2.1, 2.1)	0.99
Patients failing to clear who made a planned exit from the trial	3.8 (16)	3.0 (21)	0.7 (-1.5, 2.9)	0.50
Change in PASI				

All patients failing to clear	3.6	2.9	0.7	
Patients failing to clear who made a planned exit from the trial	4.5	2.8	1.7	

Number remaining clear

	TL-01	**UV6**
3 months		
Number assessed	25	18
Number clear (% of those who cleared) (% of those assessed)	4 (14.3) (16)	8 (40) (44.4)
6 months		
Number assessed	19	13
Number clear (% of those who cleared) (% of those assessed)	1 (3.6) (5.3)	0

Withdrawal due to toxicity

Side effect	**TL01 (n=50)**		**UV6 (n=50)**	
	Occurrence	**Withdrawal**	**Occurrence**	**Withdrawal**
Erythema	43	0	42	0
Polymorphic light eruption	3	2	1	0

Pruritus	0	0	2	1
Inflammatory psoriasis	1	1	1	1

- **TL-01: 2** missed treatments because of erythema
- **UV6:** 3 missed treatments because of erythema

Summary

- No significant difference was found in the proportion of patients achieving clearance and side effects, including the development of erythema during phototherapy, were similar for the two lamp types.

H.8.2 Narrow-band UVB vs broad-band UVB (within-patient randomisation)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of fundin g
E. Picot, L. Meunier, M. C. Picot-Debeze, J. L. Peyron, and J.	RCT – within patient design (vertical side of the body)	Total N: 21 **Drop-outs (don't complete the**	**Inclusion criteria:** Widespread and symmetrical psoriasis **Exclusion criteria:** history of photo-aggravated psoriasis	N=15 **Selective broadband UVB (TL-12),**	N=15 **Narrow-band UVB (Tl-01), three-times**	Tx max 10 weeks	**1° outcome:** change in PASI (from baseline to 10th and 20th exposure)	None stated

<table>
<tr>
<td>Meynadier. Treatment of psoriasis with a 311-nm UVB lamp. Br.J.Dermatol. 127 (5):509-512, 1992.

Ref ID: PICOT1992</td>
<td>Single-centre, France

Jan-June 1990

• Randomised (method unclear)
• No explicit ‘washout’ or run-in period (but see exclusion criteria)
• Observer blinded
• Allocation concealment not mentioned
• Sample size calculation not mentioned
• ITT analysis not mentioned
• Drop-outs/withdrawals due to AEs: unclear</td>
<td>study):
6</td>
<td>Note: none had received UVB, PUVA or retinoids in the preceding 3 months

<table>
<tr><th>Mean baseline</th><th>All (n=15)</th></tr>
<tr><td>Mean age – years (range)</td><td>46.5 (24-81)</td></tr>
<tr><td>Gender M/F</td><td>53.3%/46.7%</td></tr>
<tr><td>Psoriasis phenotype
- Plaque
- plaque/guttate
- guttate</td><td>
6
5
4</td></tr>
<tr><td>Mean duration of disease; years (range)</td><td>11.8 (4 months – 28 years)</td></tr>
</table>
</td>
<td>three-times weekly

Administered using whole-body exposure units fitted with 12 fluorescent lamps (untreated side of the body covered with thick material preventing UV penetration)

Dose determined by minimal erythematic dose (MED) measurement

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BOTH ARMS: stepped Tx strategy</td>
<td>weekly

Administered using whole-body exposure units fitted with 12 fluorescent lamps (untreated side of the body covered with thick material preventing UV penetration)

Dose determined by minimal erythematic dose (MED) measurement with TL-12 lamps

Thus, the applied doses in each cabin were not associated with the same risk of</td>
<td></td>
<td>2° and other outcomes: burning (arbitrary 0-3 scale), pruritus, cumulative dose</td>
<td></td>
</tr>
</table>

				Initial dose 70% MED with TL-12, increased exposure time by 40% if previous exposure produced no perceptible effect. Increases were reduced if erythema occurred Maximum exposure time 16 mins	*erythema* ---------- **BOTH ARMS:** The only topicals permitted were pure Vaseline or 1% salicylic acid in petroleum permitted			

Effect Size

Outcomes

Outcome	**TL01** **(N=15)**	**UV6** **(N=15)**	**p-value**

Mean PASI at baseline	27.9	27.6	NS
Mean PASI (after 10 exposures)	12.9	12.5	NS
Mean PASI (after 20 exposures)	6.6	7.8	<0.01
Mean change in PASI	21.3	19.8	
Mean score burning	0.33	2.1	<0.001

Summary

- TL01 lamps have superior efficacy and tolerance to TL-12

H.8.3 PUVA vs UVB (between-patient randomisation)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
S. S. P. Yones. Randomized double-blind trial of the	RCT Single-centre	Total N: 93 **Drop-outs (don't**	**Inclusion criteria:** Chronic plaque psoriasis, moderate-to-severe disease (PASI >7; BSA rule of nines ≥8%); ≥18 and ≤70 years of age	N=43 **PUVA (oral 10**	N=45 **NB-UVB**	Max 30 Tx + 12 months	**1° outcome:** PASI; Physician's Global Evaluation	None stated

<table>
<tr>
<td>treatment of chronic plaque psoriasis: Efficacy of psoralen-UV-A therapy vs narrowband UV-B therapy. Arch.Dermatol. 142 (7):836-842, 2006.

Ref ID: YONES2006</td>
<td>(hospital phototherapy unit), UK

Recruited April 2002 – March 2004

• Randomised (sequentially-numbered list)
• “Washout” for systemic and topical anti-psoriatic agents (see exclusion criteria)
• Assessor and patient blinded
• Allocation concealment (unclear)
• Sample size calculation based on 80% power to detect</td>
<td>complete the study):

N=6 drop-outs in PUVA arm: 1 had inadequate response; 3 for logisitic reasons; 2 for adverse events

N=16 drop-outs in NB-UVB arm: 9 had inadequate response; 3 for logisitic reasons; 3 for adverse events; 1</td>
<td>Exclusion criteria: pregnant or breastfeeding women, history of skin malignancies or photosensitivity; renal or hepatic disease; photosensitising agents in previous 4 weeks; topical antipsoriatic treatments in previous 4 weeks or systemic antipsoriatic treatments in previous 3 months; phototherapy up to 3 months before study entry or >150 sessions in lifetime.

Note: allocation stratified by:
• skin type (I/II, III/IV or V/VI)

<table>
<tr><th>Baseline</th><th>PUVA (n=43)</th><th>NB-UVB (n=45)</th></tr>
<tr><td>Median age – years (range)</td><td>44 (18-70)</td><td>40 (21-70)</td></tr>
<tr><td>Gender M/F (%)</td><td>72/28</td><td>73/27</td></tr>
<tr><td>Previously treated with PUVA, BB</td><td>44</td><td>26</td></tr>
</table>
</td>
<td>mg 8-MOP tablets – total dose 25 mg/m^2 total BSA; in case of nausea switched to 20-mg 5-MOP tablets at dose of 50 mg/m^2), twice weekly

Administered using cabin fitted with 40 (100W UVA) fluorescent tubes

Dose determined by minimal erythema dose (MED) and minimum phototoxic dose (MPD) measurement judged visually 96 h after irradiation of unaffected upper buttock</td>
<td>(+placebo tablet), twice weekly

Administered using UV5000 cabin fitted with 24 100W NB-UVB fluorescent tubes (emitting 311-313 nm)

Dose determined by minimal erythema dose (MED) and minimum phototoxic dose (MPD) measurement judged visually 24 h after irradiation of unaffected upper buttock skin surfaces.

In 3 patients</td>
<td></td>
<td>(0-6; clear, almost clear, mild, mild-to-moderate, moderate, moderate-to-severe, severe)

2^o and other outcomes: DLQI, visual analogue scale (0-10; “At the moment how would you rate your psoriasis?”) ; relapse

Relapse: recurrence of psoriasis with a PASI of 50% or more of baseline</td>
<td></td>
</tr>
</table>

	change in number of exposures of 25% at 5% significance • Reported as ITT analysis • N=5 drop-outs/withdrawals due to AEs (n=2 PUVA, N=3 NB-UVB)	lost to follow-up (unknown reason)	<table><tr><td>or NB UVB (%)</td><td></td><td></td></tr><tr><td>Median baseline PASI (range)</td><td>11.0 (8.0-30.0)</td><td>10.6 (8.0-27.9)</td></tr><tr><td colspan="3">Skin type, n (%)</td></tr><tr><td>I-II</td><td>26 (60)</td><td>17 (38)</td></tr><tr><td>III-IV</td><td>11 (26)</td><td>17 (38)</td></tr><tr><td>V-VI</td><td>6 (14)</td><td>11 (24)</td></tr></table> The 2 groups were similar for baseline characteristics	skin surfaces. In 3 patients initial dose determined using a skin-type based method ---------- **BOTH ARMS: stepped Tx strategy** Initial dose 70% MED or MPD, increased 20% at each visit (if tolerated) up to 5 J/cm^2 (UVB)or 15 J/cm^2 (PUVA); dose increments postponed if erythema developed	initial dose determined using a skin-type based method ---------- **BOTH ARMS:** all patients used aqueous cream twice daily and a bath emollient daily throughout therapy and follow-up. All wore eye protection for 12 h after treatment. Unaffected skin was covered with clothing during therapy Treatment terminated at			

					clearance; minimal improvement after 16 Tx; very slow progress after 16 treatments; intolerance to therapy; completion of 30 Tx Those who cleared followed-up every month for 1 year or until relapse (recurrence of psoriasis with PASI ≥50% of baseline)			

Effect Size

Outcomes (ITT population - included all patients)

Outcome	**PUVA** **(N=43; ITT)**	**NB-UVB** **(N=45; ITT)**	**All**	**p-value**

Clearance (%)				
Skin types I-II III-IV V-VI	 81 91	 65 65	 74% 75% 24%	
Clearance (n)				
Skin type I-IV (ITT)	31/37	22/34		
Skin type V-VI (ITT)	3/6	1/11		
Skin type I-VI (ACA)	34/38	23/38		
Median treatments to clearance	17.0	28.5		<0.001
Median change in PASI (among those with skin type I-IV; ITT) Baseline After 8 treatments Change	N=37 11 (8.0-30.0) 4.2 (0-9.3) -6.8	N=34 9.6 (8.0-27.9) 5.7 (0-21.5) -3.9		 0.001
Change in DLQI	Data given graphically (greater reduction for PUVA)			0.02
Cumulative dose (J/cm^2)	126	41.3		ND

Note: superiority of PUVA did not vary according to initial severity of psoriasis (dichotomised as PASI <10.8 vs ≤10.8)

Adverse events

Erythema (any grade)	**PUVA (N=43; ITT)**	**NB-UVB (N=45; ITT)**	**All**
Skin types, n (%)			
All I-II III-IV V-VI	21 (49**%**) 65**%** 27**%** 17**%**	10 (22**%**) 29**%** 12**%** 27**%**	35**%**
Grade 2 erythema	14%	7%	

2 patients changed from 8-MOP to 5-MOP due to nausea

Relapse rate (57/88 who cleared followed-up until relapse or max of 12 months; 3 lost to follow-up)

	PUVA (N=34)	**NB-UVB (N=23)**	**All p-value**

Still in remission at 6 months	23/34	8/23	0.02
Median time to relapse (months)	8	4	0.03

Withdrawal due to toxicity

- **PUVA:** 1 erythema; 1 itch
- **NB-UVB:** 2 erythema; 1 polymorphic light eruption

Summary

- Patients with skin types V and VI had a lower rate of clearance than those with skin types I through IV.
- In patients with skin types I through IV,PUVA was significantly more effective than NB-UVB at achieving clearance.
- The median number of treatments to clearance was significantly lower in the PUVA group.
- Six months after the cessation of therapy, 68% of PUVA-treated patients were still in remission vs 35% of NB-UVB–treated patients.
- **PUVA achieves clearance in more patients with fewer treatment sessions and results in longer remissions than NB-UVB**

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of fundin g
P. S. Chauhan, I. Kaur, S. Dogra, D. De, and A. J.	RCT	Total N: 51 **Drop-outs**	**Inclusion criteria:** plaque psoriasis, (BSA >20%); skin types IV and V	N=25	N=26	Maximu m 4 months	**1° outcome:** PASI **2°**	None stated

<table>
<tr>
<td>Kanwar. Narrowband ultraviolet B versus psoralen plus ultraviolet A therapy for severe plaque psoriasis: an Indian perspective. Clin.Exp.Dermatol. 36 (2):169-173, 2011.

Ref ID: CHAUHAN2011</td>
<td>India

• Randomised (computer-generated random numbers)
• “Washout” for systemics 4 wk and topicals 2 weeks
• Unclear blinding
• Allocation concealment (no)
• Sample size calculation: no
• Reported as ACA</td>
<td>(don’t complete the study): 7

4 in NBUVB and 3 in PUVA group (reasons unclear)</td>
<td>Exclusion criteria: those recommended for PUVA or NBUVB plus pustular psoriasis or erythroderma.

<table>
<tr><th>Mean baseline</th><th>NBUVB (n=26)</th><th>PUVA (n=25)</th></tr>
<tr><td>Age – years (±SD)</td><td>33.3 ±14</td><td>38.1 ± 12.1</td></tr>
<tr><td>Gender M/F (%)</td><td>80/20</td><td>81.8/18.2</td></tr>
<tr><td>Duration – years (±SD)</td><td>7.9±5.2</td><td>7.4±5</td></tr>
<tr><td>PASI (±SD)</td><td>15.8±2.9</td><td>16.9±4.7</td></tr>
</table>
</td>
<td>PUVA (oral methoxsalen 0.6 mg/kg), three-times weekly

Administered on non-consecutive days with UVA exposure 2h after methoxsalen

No minimum phototoxic dose (MPD) measurement was performed

Initial dose determined using a skin-type based method; 2.0 J/cm^2 for skin type IV and 2.5 J/cm^2 for skin type V</td>
<td>NB-UVB, three-times weekly

Administered on non-consecutive days

No minimal erythema dose (MED) estimation performed.

Standard starting dose of 280 mJ/cm^2 and dose increased 20% at each visit, depending on erythema, pruritus and burning sensation

----------</td>
<td>on treatment (+1-6 months post treatment)</td>
<td>outcomes: relapse (50% of baseline PASI)</td>
<td></td>
</tr>
</table>

				UVA dose increased by 1-1.5 J/cm^2 at every second visit ---------- **BOTH ARMS:** No concomitant treatment allowed except emollients and anti-histamines	**BOTH ARMS:** Treatment terminated at PASI75 or after 4 months; if no improvement in severity seen after 6 weeks treatment was terminated early and considered a treatment failure After completion of active treatment period, followed-up for 1-6 months to assess time to relapse (recurrence of psoriasis with PASI ≥50% of baseline)			

Effect Size

Outcomes (ACA population)

Efficacy at end of treatment

Outcome	**NB-UVB (N=21)**	**PUVA (N=22)**	**p-value**
PASI75	17 (80.9%)	18 (81.1%)	NS
Mean time to PASI75, weeks	9.9 ± 3.3	9.9 ± 3.5	NS
Mean treatments required to PASI75	29.6 ± 9.8	29.8 ± 10.6	
Total UV dose required for PASI75 (J/cm^2)	30.1 ± 19.5	93.8 ± 51.8	

Relapse rate by 6 months

Outcome	**NB-UVB (N=15)**	**PUVA (N=14)**	**p-value**
No longer in remission	11 (73.3%)	8 (57.1%)	NS

Summary

- PUVA and NBUVB seem to be equally effective in achieving clearance and maintaining remission of severe chronic plaque psoriasis in patients with Fitzpatrick skin type 4 and 5

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
S. Dayal, Mayanka, and V. K. Jain. Comparative evaluation of NBUVB phototherapy and PUVA photochemotherapy in chronic plaque psoriasis. *Indian J.Dermatol.Venereol.Leprol.* 76 (5):533-537, 2010. Ref ID:	RCT Single-centre (outpatient), India Recruited Feb 2004 – May 2005 • Randomised (day of the week) • "Washout" for anti-psoriatic agents (see	Total N: 60 **Drop-outs (don't complete the study):** unclear	**Inclusion criteria:** Chronic plaque psoriasis, BSA rule of nines ≥25%); ≥16 and ≤60 years of age **Exclusion criteria:** pregnant or breastfeeding women, history of skin malignancies or photosensitivity; renal or hepatic disease; previous failure or intolerance of phototherapy; any antipsoriatic treatments in previous 4 weeks **Note:** local population skin type IV or V: **Mean** / **PUVA** / **NB-UVB**	N=30 **PUVA (oral 8-MOP tablets 2h before light – total dose 0.6 mg/kg) twice weekly (non-consecutive days)** Administered using V-care UVA unit Standard initial	N=30 **NB-UVB/TL-01, twice weekly (non-consecutive days)** Administered using V-care NBUVB unit Standard initial dose:	3 months (or until PASI75)	**1° outcome:** PASI75 (remission) **2° and other outcomes:** cumulative clearance dose; number of treatments for clearance; grade I or II erythema; pruritus	None stated

<table>
<tr>
<td>DAYAL2010</td>
<td>exclusion criteria)
• Blinding unclear
• Allocation concealment (unclear)
• No sample size calculation
• ITT analysis unclear
• Dropouts unclear</td>
<td></td>
<td>
<table>
<tr><th>baseline</th><th>(n=30)</th><th>(n=30)</th></tr>
<tr><td>Mean age (years)</td><td>32.45</td><td>32.1</td></tr>
<tr><td>Gender M/F (%)</td><td>73/27</td><td>60/40</td></tr>
<tr><td>BSA 25-50%, n</td><td>19</td><td>21</td></tr>
<tr><td>BSA 50-75%, n</td><td>11</td><td>9</td></tr>
<tr><td>Disease duration (range)</td><td>6 months – 30 years</td><td>6 months-27 years</td></tr>
</table>

The 2 groups were similar for baseline characteristics</td>
<td>dose: 2 J/cm^2

BOTH ARMS: stepped Tx strategy

Initial dose increased 20% at each visit; if symptomatic erythema developed dose decreased by 50% and then increased by 10% at each subsequent visit</td>
<td>280 mJ/cm^2</td>
<td></td>
<td>PASI measures at baseline, 4, 8 and 12 weeks</td>
<td></td>
</tr>
<tr>
<td colspan="7">Effect Size

Outcomes

<table>
<tr><th>Outcome</th><th>PUVA</th><th>NB-UVB</th><th>p-value</th></tr>
</table>
</td>
</tr>
</table>

	(N=30)	**(N=30)**	
Change in PASI			
Baseline (mean ± SD; range)	21.6 ± 4.42 (16.4-34.8)	16.82±3.90 (12.2-30.6)	>0.05
After 3 months (mean ± SD; range)	1.39±0.78 (0-2.6)	1.6 ± 1.2 (0-3.2)	>0.05
Mean change	-20.21	-15.22	
PASI75 (n)	30	30	<0.05
Days to clearance (mean ± SD; range)	49.2±20.8 (35-80)	65.6±14.59 (45-86)	<0.05
Mean cumulative dose to clearance (J/cm^2)	7.4	1.16	
Mean number of treatments ± SD (range)	12.7±4.99 (6-26)	16.4±4.13 (10-32)	

Adverse events	**PUVA (N=30)**	**NB-UVB (N=30)**
Grade 1 erythema	100%	100%
Grade 2 erythema	70%	40%
Pruritus	80%	
Nausea and vertigo	75%	30%
Diffuse hair fall	70%	30%

Headache	90%	45%

Summary

- Patients of both NBUVB and PUVA groups achieved >75% clearance or complete clearance at the end of 3 months of therapy
- PUVA group achieved faster clearance, required significantly fewer number of treatment sessions and fewer number of days to clear
- However, the mean cumulative clearance dose and adverse effects were lower in the NBUVB group than in the PUVA group.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
T. Markham, S. Rogers, and P. Collins. Narrowband UV-B (TL-01) phototherapy vs oral 8-methoxypsoralen psoralen-UV-A for the treatment of	RCT Single-centre (phototherapy unit), Ireland Recruited Jan 1999 – June 2000	Total N: 54 **Drop-outs (don't complete the study):** N=5 drop-outs in TL01 arm: 4 defaulted and 1	**Inclusion criteria:** Chronic plaque psoriasis affecting trunk and limbs, extent on trunk and limbs by rule of nines ≥8%); no antipsoriatic treatment within 2 weeks prior to study or phototherapy 4 months beforehand; ≥16 years of age; skin types I-III **Exclusion criteria:** pregnant or breastfeeding women; active systemic therapy for psoriasis within previous 8 weeks; abnormal photosensitivity; renal or hepatic	N=25 **PUVA (oral 8-MOP crystalline tablets 2h before light – total dose 0.6 mg/kg; those who could not tolerate 8-MOP were given 5-MOP 1.2 mg/kg)**	N=29 **NB-UVB/TL-01, three-times weekly** Administered using whole-body cabin with	Tx + 12 months	**Outcomes:** number of treatments to clear, number of days in treatment, number of days in remission, and adverse	None stated

<table>
<tr>
<td>chronic plaque psoriasis. Arch.Dermatol. 139 (3):325-328, 2003.

Ref ID: MARKHAM2003</td>
<td>• Randomised (unclear method)
• “Washout” for anti-psoriatic agents (see exclusion criteria)
• Observer blinded
• Allocation concealment (unclear)
• Sample size calculation based on 80% power to detect change in number of exposures of 25% at 5% significance (2 groups of 50 patients required – power not reached)
• No ITT analysis (only available cases</td>
<td>withdrawn because of flaring and required in-patient admission

N=4 drop-outs in PUVA arm: 2 defaulted and 2 withdrawn because of flaring and required in-patient admission</td>
<td>disease; previous failure or intolerance of phototherapy; any antipsoriatic treatments in previous 4 weeks
<table>
<tr><th>Mean baseline</th><th>PUVA (n=25)</th><th>NB-UVB (n=29)</th></tr>
<tr><td>Mean age, years (range)</td><td>39 (28.5-52)</td><td>36 (27-50)</td></tr>
<tr><td>Gender M/F (%)</td><td>52/48</td><td>58.6/41.4</td></tr>
<tr><td>Skin type
I
II
III</td><td>
4
11
10</td><td>
3
13
13</td></tr>
<tr><td>Extent, mean (range), %</td><td>15 (10-25.5)</td><td>13.9 (12.2-17.5)</td></tr>
<tr><td>PASI score, mean (range)</td><td>15.2 (10.8-18.9)</td><td>13.9 (12.2-17.5)</td></tr>
<tr><td>Previous phototherapy</td><td>18</td><td>17</td></tr>
</table>
</td>
<td>twice weekly (non-consecutive days)

Administered using whole-body cabin with 40 UVA fluorescent lamps (315-400 nm)

Dose determined by minimal phototoxic dose (MPD) measurement judged visually 72 h after irradiation of 8 unaffected regions of the upper back.

Wore UVA protective glasses for 24 h after treatment</td>
<td>24 TL01 fluorescent lamps (311-313 nm)

Dose determined by minimal erythematic dose (MED) measurement judged visually 24 h after irradiation of 8 unaffected regions of the upper back.

BOTH ARMS:

Aqueous cream</td>
<td></td>
<td>effects.

The end point of the study was complete clearance of psoriasis.</td>
<td></td>
</tr>
</table>

	analysed) • Dropouts due to AEs: unclear		The 2 groups were similar for baseline characteristics	---------- **BOTH ARMS: stepped Tx strategy** Initial dose 70% MED or MPD, increased 20% at each treatment (dose increments postponed if erythema developed; grade 2 or 3 erythema = next exposure postponed)	allowed as required; Vioform HC cream applied twice daily to flexural psoriasis and tar pomade was applied to the scalp Patients were reviewed once weekly during the study and monthly after clearance for 12 months Relapse was defined as 50% of the original extent.			

Effect Size

Outcomes (for 45 who completed treatment)

Outcome	**PUVA (N=21)**	**NB-UVB (N=24)**	**p-value**
Median number of treatments to clearance (95% CI)	19 (14.6-25.0)	25.5 (18.0-32.5)	0.03
Median days to clearance (95% CI)	66 (52.0-92.6)	67 (47.9-81.7)	0.46
	N=19	**N=24**	
Median duration of remission/ time to relapse (days) (95% CI)	231 (162.7-365.0)	288.5 (170.6-365.0)	0.40
Months in remission; n (%)			
3	18 (95)	23 (96)	
6	13 (68)	16 (67)	
9	8 (42)	23 (96)	
12	10 (42)	7 (37)	

Adverse events	**PUVA (N=21)**	**NB-UVB (N=24)**

Grade 1 erythema	80%	75%
Grade 2 erythema	40%	0%
Pruritus	"Equal"	
Polymorphic light eruption	"Equal"	
Nausea	~15% (presented graphically)	0%

Summary

- Those in the PUVA group required significantly fewer treatments to clear.
- There was no significant difference in the number of days to clear or number of days in remission.
- A similar percentage of patients in the TL-01 and PUVA groups developed minimal perceptible erythema, showing that the regimens were equally erythemogenic. Asymptomatic, well-defined erythema occurred only in the PUVA group.
- **Narrowband UV-B phototherapy, used 3 times weekly, is as effective for the treatment of CPP as oral 8-MOP PUVA used twice weekly**

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
A. B. Serwin and B. Chodynicka. Soluble	RCT (plus control group)	Total N: 50 **Drop-outs (don't**	**Inclusion criteria:** Early onset (before 40 years of age) plaque-type psoriasis; skin type II or III	N=25	N=25	20 Tx + 1 month follow-up	**1° outcome:** serum concentration sTNF-R1	None stated

<table>
<tr>
<td>tumour necrosis factor-alpha receptor type 1 as a biomarker of response to phototherapy in patients with psoriasis. Biomarkers 12 (6):599-607, 2007.

Ref ID: SERWIN2007</td>
<td>Single-centre, Poland

Recruited Jan–Sept 2005

• Randomised (unclear method)
• No washout period
• Blinding not stated
• Allocation concealment (unclear)
• No sample size calculation
• ITT analysis
• Dropouts due to AEs: 0</td>
<td>complete the study): 0</td>
<td>Exclusion criteria: concomitant systemic disorders

<table>
<tr><th>Mean baseline</th><th>PUVA (n=25)</th><th>NB-UVB (n=25)</th></tr>
<tr><td>Mean age, years±SD (range)</td><td>43.40±12.18 (22-59)</td><td>38.21±11.40 (21-60)</td></tr>
<tr><td>Gender M/F (%)</td><td>56/44</td><td>44/56</td></tr>
<tr><td>Mean age of onset of psoriasis, years±SD (range)</td><td>22.93±8.71 (10-40)</td><td>18.89±11.11 (4-40)</td></tr>
<tr><td>PASI score (range)</td><td>11.40-24.61</td><td>7.11-23.40</td></tr>
</table>

The 2 groups were similar for baseline characteristics</td>
<td>PUVA (oral 8-MOP soft gelatine capsules 1h before light – total dose 0.6 mg/kg; three-times weekly (up to 20 irradiations); non-consecutive days

Administered using Arimed PUVA lamps (320-340 nm)

Initial dose: 70% MPD</td>
<td>NB-UVB three-times weekly (up to 20 irradiations); non-consecutive days

Administered using TL01 lamps (311-313 nm)

Initial dose: 50% MED

BOTH ARMS:

Only topical emollients permitted</td>
<td></td>
<td>(including from 20 controls – healthy volunteers)

2° and other outcomes:

PASI75 and change in PASI</td>
<td></td>
</tr>
</table>

Effect Size

Outcomes (ITT analysis)

PASI score (mean±SD)	**PUVA (N=25)**	**NB-UVB (N=25)**	**p-value**
Baseline	17.22±3.48	16.32±5.26	NS
After 10 treatments	11.23±3.39	8.57±3.33	<0.01
After 20 treatments	5.55±2.10	4.42±1.67	<0.05
1 month after end of treatment	4.85±1.79	4.50±1.60	NS
PASI75 after 20 treatments, n (%)	**19 (76%)**	**21 (84%)**	**p>0.05**

Summary

- Narrowband UV-B and PUVA gave similar therapeutic results after 20 treatments

<table>
<tr><th>Reference</th><th>Study type</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of fundin g</th></tr>
<tr>
<td>A. Akman, O. Dicle, F. Yilmaz, M. Coskun, and E. Yilmaz. Discrepant levels of vascular endothelial growth factor in psoriasis patients treated with PUVA, Re-PUVA and narrow-band UVB. Photodermatol.Photoimmunol.Photomed. 24 (3):123-127, 2008.

Ref ID: AKMAN2008</td>
<td>RCT

Single-centre (dermatology out-patient clinic), Turkey

• Randomised (unclear method)
• No washout period
• Blinding not stated
• Allocation concealment (unclear)
• No sample size calculatio</td>
<td>Total N: 40

Drop-outs (don’t complete the study): 2 – due to side effects or lost to follow-up

PUVA: 2

NB-UVB: 0</td>
<td>Inclusion criteria: Topical or systemic therapy for at least 2 months

Exclusion criteria: not stated

<table>
<tr><th>Mean baseline</th><th>PUVA (n=18)</th><th>NB-UVB (n=20)</th></tr>
<tr><td>Mean age, years±SD</td><td>38.8±15.0</td><td>42.6±14.0</td></tr>
<tr><td>Gender M/F (%)</td><td>28/72</td><td>40/60</td></tr>
<tr><td>Mean PASI ±SD</td><td>15.8±8.2</td><td>10.5±6.5</td></tr>
</table>
</td>
<td>N=20

PUVA three-times weekly

Initial dose: determined by Fitzpatrick skin type

Dose escalation: increased by 30% of initial dose at each session</td>
<td>N=20

NB-UVB three-times weekly

Initial dose: 70% MED
Dose escalation: 20% increment at each session

N=20</td>
<td>8 weeks (24 sessions)</td>
<td>1° outcome: Change in PASI

2° and other outcomes:
Serum VEGF</td>
<td>None stated</td>
</tr>
</table>

	n • No ITT analysis (only available cases analysed) • Dropouts due to AEs: unclear							

Effect Size

Outcomes (ACA)

PASI score (mean±SD)	**PUVA (n=18)**	**NB-UVB (n=20)**
Baseline	15.8±8.2	10.5±6.5
After 10th day of treatment	12.6±1.6	9.23±1.33
After 12 treatments	8.71±1.59	7.1±1.0
After 24 treatments	3.4±0.7	3.9±0.7
Mean change (all P<0.001)	**-12.4**	**-6.6**

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
P. M. Gordon, B. L. Diffey, J. N. Matthews, and P. M. Farr. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. *J.Am.Acad. Dermatol.* 41 (5 Pt 1):728-732, 1999. Ref ID: GORDON1	RCT Single-centre (referred to PUVA clinic), UK Referred July 1996-Sept 1997 • Randomised (randomised permuted blocks within strata) • Washout period (emollient alone in 4 weeks before	Total N: 100 **Drop-outs (don't complete the study):** TL01: 4 4 = failure to attend PUVA: 5 2 = failure to attend; 2 = withdrew due to nausea; 1 = general health problem	**Inclusion criteria:** Chronic plaque psoriasis (moderate-to-severe) **Exclusion criteria:** current systemic therapy for psoriasis; any UV therapy within the preceding 6 months **Note:** allocation stratified by: • plaque size (small <3 cm diameter) or large (>3 cm diameter) • skin type (I/II or III/IV) **Mean baseline** / **PUVA (n=49)** / **TL01 (n=51)** Mean age (SD): 41.0 (11.2) / 43.3 (12.9) **Skin phototy**	N=49 **Oral PUVA twice weekly** Psoralen: microcrystalline methoxsalen; 25 mg/m^2 total BSA (range 30-60 mg; median 40 mg) Administered using whole-body units fitted with 40 fluorescent PUVA lamps Minimal phototoxic dose (MPD) measurement 2 h	N=51 **NB-UVB (TL01) twice weekly** Administered using whole-body units fitted with 40 fluorescent TL01 lamps Dose determined by minimal erythematic dose (MED) measurement judged visually 24 h after irradiation of	Tx + 6 months in those who cleared Patients withdrawn if no improvement after 16 Tx	**1° outcome:** clearance of plaques at all sites above knees (nearly clear) **2° and other outcomes:** number of treatments for clearance; UV dose for clearance; adverse effects; relapse rate Assessments made by clinician after every	None stated

999	treatment) • Assessor blinded • Allocation concealment (sealed envelopes) • Sample size calculation based on 80% power to detect change in median exposure of 25% at 5% significance (2 groups of 50 patients required • ITT analysis • Dropouts due to AEs: PUVA: 2; TL01: 0		**pe (n)** I II III IV Small plaque psoriasis Large plaque psoriasis	 8 18 16 7 28 21	 5 21 24 1 29 22	after psoralen ingestion judged visually 72 h after irradiation of the forearm (4 test doses); initial dose on same day as phototesting 1-2.5 J/cm^2 based on PUVA history, skin type, and experience of sunburn. Dose then increased stepwise to MPD if tolerated or to a maximum of 6 J/cm^2; subsequently weekly dose increments used starting with 40%, reducing stepwise to 10% by sixth week --- **BOTH ARMS:** dose increments postponed or treatments missed	forearm (10 test doses) **Initial dose:** 70% MED **Dose escalation:** increased by 30-40% each week, reducing stepwise to 5-10% by 6th week (max dose 2066 mJ/cm^2)		8 Tx (or sooner if nurses suspected clear)	

				in case of erythema				

Effect Size

Outcomes (ITT analysis n=100)

Outcomes	PUVA (n=49)	TL01 (n=51)	OR (95% CI)	p-value
Clear (n)	41 (84%)	32 (63%)	3.04 (1.18-7.84)	0.018
Treatment stopped owing to poor response (after 16 Tx), n	3	15		
Median number of exposures for clearance (based on Weibull distribution)	16.7	25.3	Ratio of medians: 1.52 (1.24-1.86)	<0.001
Erythema	17	37		
Erythema requiring missed Tx	6	1		
Nausea	2	0		

Relapse rate (no longer clear)/time to relapse of those cleared (after stopping UV treatment)

	TL-01	PUVA

Failed to clear	19 (38%)	8 (18%)
Clear but relapsed at 3 months	19 (38%)	14 (32%)
Clear at 3 months but relapsed at 6 months	5 (10%)	5 (11%)
Clear at 6 months	7 (14 %)	17 (39%)
Total	50	44

- Cumulative proportional odds model showed a significant difference between the treatments
- Odds of failing to clear at each of the trial assessment points (end of Tx; 3 moths and 6 months) were 3.69 times higher for TL01 than PUVA (95% CI: 1.61-8.47)

Conclusion

- Twice weekly oral PUVA is more efficacious than twice weekly TL01; clearance of psoriasis achieved in a significantly greater proportion of patients treated with PUVA than TL01 and significantly fewer treatments were needed for clearance with PUVA

H.8.4 PUVA vs UVB (within-patient randomisation)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
R. S. Dawe, H. Cameron, S. Yule, I. Man, N. J. Wainwright, S. H. Ibbotson, and J. Ferguson. A randomized controlled trial of narrowband ultraviolet B vs bath-psoralen plus ultraviolet A photochemotherapy for psoriasis. *Br.J.Dermatol*. 148 (6):1194-1204, 2003.	RCT – **within-patient randomisation** Single-centre (referred from general dermatology clinics), Scotland Referred September 1996-May 1999 • Randomised (random number generation	Total N: 28 **Drop-outs (don't complete the study):** 10 4 = inadequate response on PUVA side 1=inadequate response on NBUVB 2 = PLE requires topical steroids 1 = illness 1 = PUVA	**Inclusion criteria:** Chronic plaque psoriasis **Exclusion criteria:** age <18 years, history of skin cancer or keratoses; phototherapy, PUVA or systemic therapy for psoriasis within the preceding 3 months **Mean baseline** / **All (n=28)** Age (range) / 22-71 Gender M/F (%) / 61.7/39.3 **Skin phototype (n)** I / 6 II / 12	N=28 **Bath PUVA twice weekly** Psoralen: TMP 50 mg in 100ml ethanol mixed in 150 l 37C bathwater to make a concentration of 0.33 mg/l. Patient soaked in bathwater for 10 minutes followed by immediate exposure to UVA Administered using Dixwell cabinet fitted with 47 R-	N=28 **NB-UVB (TL01) three-times weekly** Administered using either Waldmann UV5000 cabinet fitted with 24 100W TL01 lamps or Ninewells Medical Physics department cabinet fitted with	Tx + 1 year (or until relapse) in those who cleared/had MRA on both sides End points: clearance (no palpable psoriasis) or minimal residual activity (MRA; trace disease, below knees or on sacrum only); or 30 treatments on both sides	**1° outcome:** days and number of Tx to clear **2° and other outcomes:** Adverse events, duration of remission Severity of psoriasis assessed before Tx and at each Tx visit on 0-4 scale for each of scaling,	None stated

Ref ID: DAWE2003	) • Washout period • Assessor blinded (assessment of AEs by unblinded nurse) • Allocation concealment (sequentially numbered allocation list held by independent administrator) • Sample size calculation (power of 80% to detect either a difference of 2 Tx or of 7 days to clearance = need 22	itch 1 = pregnancy 1 = fail to attend	III: 10 Previous UVB or PUVA (n): 24 Previous UVB only: 11 Previous PUVA only: 13* Previous systemic retinoid: 2 Previous methotrexate: 1 *High proportion; not representative of psoriasis population	UVA tubes Light dose determined by minimal phototoxic dose (MPD) measurement judged visually 72 h after irradiation of 8 unaffected regions of the upper back. Wore half-body suits that allowed transmission of no UVB and negligible UVA (0.6% transmission at 365 nm) **Initial dose:** 40% MPD **Dose escalation:** increased by 20% at each session, reducing to 10%	50 100W TL01 lamps This side treated first Dose determined by minimal erythematic dose (MED) measurement judged visually 24 h after irradiation of 8 unaffected regions of the upper back. **Initial dose:** 70% MED **Dose escalation:** increased by 20% at each session,	Relapse: return of psoriasis of sufficient severity that patient was unwilling to proceed with emollient alone or increase in global score to 50% that of baseline	erythema and induration of 3 symmetrical plaques chosen at baseline on upper limbs, trunk and lower limbs A 0-4 global score was also used (no psoriasis to severe) based on PASI	

	patients; **underpowered** because only 18 completed) • Per protocol comparison for those who reached clearance or MRA • ITT analysis (using Cox's proportional hazards – assumes outlook for those who withdrew was the same as for those who did not withdraw) • Dropouts due to AEs: 3			increments (max dose 15 J/cm^2) --- **BOTH ARMS:** decision to stop treatment made by masked observer Facial protection offered if no facial psoriasis; males wore genital protection Adjunctive therapy restricted to emollients known not to significantly impede UV transmission and standard topicals for scalp, face and flexures Tx stopped when patient clear or	reducing to 10% increments (max dose 2066 mJ/cm^2)			

				after 4th exposure following first documentation of minimal residual activity				

Effect Size

Outcomes (available case analysis)

Outcomes	**PUVA side**	**NB-UVB side**	**95% CI; p-value**
Clear/MRA at completion (n)	15/22	21/23	

Outcomes (ITT analysis n=28)

Outcomes	**Hazard ratio (TL01 vs PUVA)**	**TL-01 (n=28)**	**PUVA (n=28)**	**95% CI; p-value**
Clear/MRA at completion – modelled against days to clear	3.53			1.99-6.26; <0.001
Median days to clear		61	86	
Clear/MRA at completion – modelled against Tx to clear	1.03			0.58-1.83; 0.92
Median Tx to clear		25	21	
Clear/MRA at completion (n)		**21**	**15**	6-37%; p =

				0.02
Mean time to relapse among those who cleared		**N=21** **106.72 (SD 62.71)**	**N=15** **67.45 (SD 65.62)**	**MD: 39.27 days**

Adverse events	**TL-01 (N=28)**	**PUVA (N=28)**	**95% CI; p-value**
Grade 1 erythema	16 (57%)	21 (75%)	-2 to 38%; p=0.10
Grade 2 erythema	10 (36%)	8 (29%)	-12 to 27%; p=0.48
Grade 3 erythema	4 (14%)	4 (14%)	-17 to 17%; p >0.99
Polymorphic light eruption	2 (71.4%)	2 (71.4%)	
Itch	0	1 (3.6%)	

Duration of remission

No difference between treatments in duration of remission (data presented graphically)

Conclusion

- TL01 is more efficacious than TMP bath PUVA to treat chronic plaque psoriasis

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
E Snellman, T. Klimenko, T. Rantanen Randomized Half-side Comparison of Narrowband UVB and Trimethylpsoralen Bath plus UVA Treatment for Psoriasis *Acta Derm Venereol.* 84: 132-137, 2004 Ref ID: SNELLMAN2004	RCT (right/left comparison; **within-patient randomisation**) Single-centre (referred to Dermatology Department), Finland Referred September 2001-March 2002 • Right/Left side of the body comparison of TL01 and PUVA • Randomised (automatically computed random number table)	Total N=18 **Drop-outs (don't complete the study): 3** PUVA side: 1 (exacerbation of psoriasis) Remaining 2 not related to treatment	**Inclusion criteria:** Chronic over 2 years duration, symmetric and mostly plaque type, > 18 years of age, suitable for and in need of phototherapy, skin type II-IV. **Exclusion criteria:** Systemic therapy or any UV therapy within the preceding 2 months or topical treatment in the previous 2 weeks. Scalp and face psoriasis was excluded from being assessed during the study. No individual group	N=17 **Bath PUVA three times a week** Half side irradiations: patients wore a double brown cotton material UV protective suit Psoralen: Trioxysalen alcohol solution; 50mg/100ml diluted in 150L of tap water. 0.33mg/l bath concentration. Bathing time was 10 mins. Skin Type II: Dose 0.05 J/cm^2. 20-30%	N=17 **NB-UVB (TL01) three times a week** Half side irradiations: patients wore a double brown cotton material UV protective suit UVB was given first to avoid any interaction with the Trioxysalen.	10 week treatment during the trial with a 6 month follow up period in those who cleared If treatment was unsatisfactory at the end of the 10 weeks, patients could withdraw.	**1° outcome:** Improvement in the PASI (modified PASI excluding the palms, soles, and head), GIS (Global Improvement Score) and TLS (Target Lesion Score) **2° and other outcomes:** Time to 100% relapse in the PASI or time to start another treatment (2 month interval	None stated

	• Washout period (2 months for systemic/photo therapy and 2 weeks for topicals) • Assessor blinded • Allocation concealment (sealed envelopes) • Sample size calculation based on 80% power to detect 10% difference in PASI at 5% significance (minimum 12 patients required) • ITT **but note :** One patient dropped out after randomisation so did not receive their allocated treatment or have their data collected.		baseline data apart from skin type/MED/MPD. For the 17 patients who undertook the trial: • 4 females, 13 males • Mean age 46 +/- 12 years • Severity ranged from mild to severe • Skin phototype: II n=9 , III n=5 , IV n=3 .	increases initially, then 10%. Skin Type III & IV: Dose 0.07 J/cm^2. Each dose repeated at least twice. Administered using cabinets fitted with 27 fluorescent PUVA tubes Minimal phototoxic dose (MPD) and minimal erythema dose (MED) were assessed at the beginning using geometric dose series increasing by √2. MPD measurement read at 72hrs. Maximum 30 exposures. Emollient or Salicylic acid were permitted	Administered using a cabin with 40 TL01 tubes. **Initial dose:** 50% MED **Dose escalation:** increased by 20-30% each time until erythema appeared or 1.0J/cm^2. Then increases were by 10 or 20%. Erythema development would result in reducing, keeping constant or not giving the dose.		recordings in post treatment phase) Cumulative UVB and UVA dose Adverse events Assessments made by a blinded observer at the start of the trial, then weekly for the 10 weeks. During the post-treatment follow up it was every 2 months.	

	• **Drop out due to AEs : PUVA : 1 ; TL01 : 0**			for concurrent use (not to be applied before the irradiations). In adverse events such as skin burn topical glucocorticoid formulation was permitted for 1-2 days.	Minimal phototoxic dose (MPD) and minimal erythema dose (MED) were assessed at the beginning using geometric dose series increasing by √2. MPD measuremen t read at 72hrs. Maximum 30 exposures. Emollient or Salicylic acid were permitted for concurrent use (not to			

					be applied before the irradiations). In adverse events such as skin burn topical glucocorticoid formulation was permitted for 1-2 days.			

Effect Size

Outcomes (ITT n=17)

Outcomes	**PUVA (n=17)**	**TL01 (n=17)**	**p-value**
Improvement in the PASI (modified PASI), median (range)	Initial: 8.6 (1.8-14.4) Final: 3.5 (0-9.6) Difference: 45%↓	Initial: 8.5 (1.8-15.2) Final: 1.0 (0-6.6) Difference: 77%↓ (24-100%↓)	Initial: p>0.05 Final: p<0.001

	(8-100%↓)		
Mean change in PASI	**4.44 SD: 3.83** **N=14**	**7.15 SD: 4.07** **N=14**	
Clear - 100% improvement in modified PASI (n)	1 (5.9%)	5 (29.4%)	
2 month relapse (100% PASI relapse)	7/13[1]	6/13[2]	
Relapse in 2 months to ≤ 4 months follow up	6/6 (100%)[3]	6/6 (100%)	
Median cumulative dose of UV (J/cm^2), range	8.06 (3.31-12.51)	39.92 (13.95-81.56)	
Median number of UV treatments[4], range	30 (23-30)	30 (22-30)	
Erythema	11	17	

Conclusion

- NBUVB was more effective and safer than PUVA

[1] Two patients had bilateral relapse, 4 patients used other treatments (PUVA or TL01 sides not stated) and 1 patient had a relapse on their PUVA treated side
[2] Two patients had bilateral relapse, 4 patients used other treatments (PUVA or TL01 sides not stated)
[3] 1 patient had a bilateral relapse at < 4months, 4 patients used other treatments and one patient relapsed at 4 months.
[4] Calculations exclude two patients who withdrew early from the study (moved house, deteriorated on the PUVA side)

H.8.5 Different frequencies of narrowband UVB (TL01) – between patient randomisation

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of fundin g
Z. Hallaji, M. Barzegari, K. Balighi, P. Mansoori, A. Taheri, P. Mansoori. 2010 A comparison of three times vs. five times weekly narrowband ultraviolet B phototherapy for the	RCT Single-centre (referred to Dermatology clinic), Iran Referred April 2003- October 2004 • Randomised (Weighted randomization (minimization) • Assessor blinded	Total N=65 **Drop-outs (don't complete the study):** 3 times/wk TL01: N=9 1= lost to f/u 8= withdrawal due to repeated failure to attend or inability to attend the clinic for >2wks 5 times/wk	**Inclusion criteria:** Patients with chronic plaque psoriasis affecting >10% of their body surface area **Exclusion criteria:** Patients aged <10 years old, pregnancy, history of skin cancer/solar keratoses, history of immunosuppressive therapy or phototoxic drugs, history of abnormal photosensitivity, history of previous failure or intolerance to phototherapy and patients who have had topical psoriasis therapy in the last 2 weeks, systemic treatment in the last 2 months or phototherapy in the last 4 months. Emollients or mild/mod	N=32 **NB UVB - TL01 three times a week** Petrolatum was applied to the psoriatic lesions prior to treatment. TL01 fluorescent lamps were used in the cubicles.	N=33 **NB UVB - TL01 five times a week** Petrolatum was applied to the psoriatic lesions prior to treatment. TL01 fluorescent lamps were used in the	Tx until clearance occurred (range 4.7-23 weeks) Treatment continued until clearance (above the knees) or unacceptable side effects. Treatment was stopped if deemed no further improvement could be made. Poor clearance	**1° outcome:** Proportion of patients who reached clearance[5] **2° and other outcomes:** Cumulative UVB dose Number of treatments Length of treatment period PASI score Skin erythema during treatment, postlesional hypopigmen	None stated

[5] Clearance: When all exposed psoriatic lesions above the knees had healed (flat, without scale or erythema)

<table>
<tr>
<td>treatment of chronic plaque psoriasis. Photodermatology, Photoimmunology & Photomedicine26; 10-15. 2010

Ref ID: HALLAJI2010</td>
<td>No allocation concealment
Sample size calculation based on 80% power to detect >30% difference in treatment success (clearance) at 5% significance (2 groups of 28 patients required)
ITT for clearance. For all other outcomes available cases were analysed.</td>
<td>TL01: N=11

11= withdrawal due to repeated failure to attend or inability to attend the clinic for >2wks</td>
<td>glucocorticoids on the scalp or photoprotected areas was allowed pre and during the study.

Two groups were matched for PASI, age and sex.

<table>
<tr><th>Mean baseline</th><th>TL01 3 times/wk</th><th>TL01 4 times/wk</th></tr>
<tr><td>Sex (M%)</td><td>60.9%</td><td>54.5%</td></tr>
<tr><td>Mean age (range)</td><td>32.6 (13-75)</td><td>36.1 (20-58)</td></tr>
<tr><td>Skin phototype (n)
I
II
III
IV</td><td>

0
6
13
4</td><td>

0
3
16
3</td></tr>
</table>
</td>
<td>First dose: 75mJ/cm^2

Incremental dose increase: 20% of previous dose

Effect of erythema on next dose:

Grade 1: repeat previous dose, thereafter 10% increases

Grade 2: postpone until erythema resolved. 80% previous dose, thereafter 10% increases.

Grade 3: postpone until erythema and pain resolved. 50% previous dose, thereafter 10% increases.

Missed treatments:</td>
<td>cubicles.

First dose: 75mJ/cm^2

Incremental dose increase: 20% of previous dose

Effect of erythema on next dose:

Grade 1: repeat previous dose, thereafter 10% increases

Grade 2: postpone until erythema resolved. 80% previous dose, thereafter 10%</td>
<td>withdrawal only after ≥16 exposures.</td>
<td>tation or hyperpigmentation at the site of healed psoriatic lesions Patient satisfaction with the treatment

Assessments made by clinician after 12 Tx and when the patient was clear (end of the treatment period)</td>
<td></td>
</tr>
</table>

			No significant differences were found between the two groups in their baseline/demographic variables. **Note: Adult and Child mixed population**	5-7 days: repeat previous dose 8-14 days: 75% of previous dose >14 days: withdraw patient from the study MED used was the lowest MED reported in previous papers: 75mJ/cm^2 Male patients wore genital protection. All patients were given UV protective goggles. No limit for the number of exposures.	increases. Grade 3: postpone until erythema and pain resolved. 50% previous dose, thereafter 10% increases. Missed treatments: 5-7 days: repeat previous dose 8-14 days: 75% of previous dose >14 days: withdraw patient from the study			

					MED used was the lowest MED reported in previous papers: 75mJ/cm^2 Male patients wore genital protection. All patients were given UV protective goggles. No limit for the number of exposures.			
Effect Size **Outcomes (ITT analysis n=65, ACA N=45)**								

Outcomes	**TL01 3 times a week** **(ITT n=32 , ACA n=23)** **(95% CI)**	**TL01 5 times a week** **(ITT n=33, ACA n=22)** **(95% CI)**	**p-value**
Clearance of psoriasis - ITT (non-responder imputation (n,%)	18 (56.3%)	15 (45.5%)	0.38
Clearance of psoriasis - ACA (n,%)	18 (78%) (61-95%)	15 (68%) (48-88%)	0.44
Mean number of treatments to clearance (95% CI)	35.1 (30.2-39.9) **N=18**	36.5 (31.2-41.8) **N=15**	
Mean time to clearance, weeks (95% CI)	13.7 (11.4-15.9) **N=18**	7.9 (6.7-9.0) **N=15**	
Mean cumulative UVB dose (J/cm^2) (95% CI) – ACA	43.0 (34.4-51.7)	46.3 (34.5-58.0)	0.51
Mean number of treatments (95% CI)– CA	37.6 (32.6-42.6)	37.8 (33.5-42.2)	0.95
Mean length of treatment (weeks) (95% CI) – ACA	14.7 (12.5-16.9)	8.9 (7.6-10.1)	<0.001
Mean Baseline PASI score - ACA	16.4	16.4	0.02
Mean end of treatment PASI score-ACA	1.9	4.9	

Erythema[6]			
Mild (Grade1-2)	15 (65%)	16 (73%)	0.59
Moderate (Grade 3)	0	0	

Conclusion

- **There is no significant difference for the clearance of psoriasis between TL01 3 times a week and TL01 five times a week**
- **There is a significant reduction in the number of weeks of treatment for TL01 five times a week compared to TL01 3 times a week**
- **TL01 three times a week significantly reduces the PASI score compared to TL01 five times a week**

[6] No other complication or side-effect was recorded in the study

H.8.6 Different frequencies of narrowband UVB (TL01) – within-patient randomisation

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
R. S. Dawe, N. J. Wainwright, H. Cameron, J. Ferguson. Narrow-band (TL-01) ultraviolet B phototherapy for chronic plaque psoriasis: three times or five times weekly treatment? *British Journal of Dermatology*. 138; 833-839. 1998	Paired (within patient) **right/left comparison** RCT Single-centre (referred to the dermatology outpatient clinic), UK Referred November 1995 – June 1996 • Randomised (random number table) • Unclear allocation	Total N: 21 **Drop-outs (don't complete the study): 2** 1= failure to attend (intercurrent illness) 1=declined to continue as satisfied with a modest improvement	**Inclusion criteria:** Chronic plaque psoriasis **Exclusion criteria:** history of skin cancer/ solar keratoses, on systemic immunosuppressive therapy, age <18 years old, phototherapy PUVA or any systemic therapy for psoriasis within the preceding 3 months, guttate psoriasis, known abnormal photosensitivity and any expressed hesitation about ability to attend daily treatment. **Mean** | **N=21**	N=21 **NB-UVB (TL01) three times a week** Either a UV5000 Waldmann cubicle with 24 100W TL01 lamps or a 50 100W TL01 lamps were used. --- **Both arms:**	N=21 **NB-UVB (TL01) five times a week** Either a UV5000 Waldmann cubicle with 24 100W TL01 lamps or a 50 100W TL01 lamps were used.	Treatment was stopped when the patient was clear of psoriasis or in a state of minimal residual activity (MRA) for 4 treatments. Treatment given until clearance is reached. The	**1° outcome:** clearance of psoriasis **2° and other outcomes:** Psoriasis Severity Scores (SEI) number of treatments for clearance; UV dose for clearance; number of days to clearance Relapse[7]	None stated

[7] Relapse definition: Increase in Global Score to 50% of the baseline value or an increase in the psoriasis severity that the patient is no longer willing to solely use emollient.

Ref ID: DAWE1998	concealment • Assessor blinded • No sample size calculation reported in the paper • ACA analysis and those who cleared • There were no dropouts due to adverse events		**baseline** Sex (M%) 61.9% Mean age (SD) 43 years (13.6) **Skin phototype (n)** I 2 II 14 III 5 IV 0	MED was done on the upper back skin. MED was the lowest dose that produced a just perceptible erythema. **Initial dose**: 70% of MED Max. Exposure dose: 2066mJ/cm^2 Each side was treated independently: Mon, Wed, Fri for 3x week and Mon-Fri for 5x week. Patients wore a half body suit. **Dose escalation:** No erythema- 20% increase. Mild- repeat previous dose and reduce to 10% increments. Mod- postpone 1 treatment, repeat previous dose, then 10% increments.		patient is then followed up until relapse/ for one year.	Adverse events Assessments were made at each appointment for UVB. Assessments were made by monthly telephone calls or appointments at the department for relapses.	

				Sever- no treatment. Further treatment at the doctors discretion. Maximum 30 exposures. All patients were offered facial photo-protection (faceshield) or topical sunscreen if no facial psoriasis. Emollients, aqueous cream, diprobase, coconut oil were allowed. Standard topical treatments for scalp, face and flexures were also permitted.				

Effect Size

Outcomes (ITT analysis n=21, those that cleared analysis CLA n=16)

Outcomes	**TL01 3 times a week (ITT N=21 CLA N=16)**	**TL01 five times a week (ITT N=21 CLA N=16)**	**Difference between the two treatment groups**	**OR (95% CI)**	**p-value**
Clearance of psoriasis* – ITT Clearance of psoriasis* - ACA	16/21 16/19	16/21 16/19			
Median number of days to clear (range) - CLA	40 (23-63)	35 (19-43)	5 95% CI 2-11		0.007
Median UVB dose (multiples of individuals MED) to clear (range) - CLA	64 (23-125)	94 (27-164)	95% CI 5-33		0.010
Median number of treatments to clear (range) - CLA	17	23.5	95% CI 3.5-8		0.001
Erythema – Grade 2 - CLA	3/16	15/16			<0.001
Adverse events: Polymorphic light eruption (PLE)	1	2			
Time to Relapse (topical therapy other than emollients required or fall to 50% of baseline)	Graphical representation – median = 165	No data given. Graphical representation -	9 days		0.73

	days	median = 174 days			

*Note – this was defined as clearance on both sides (unclear if any participants cleared on one side only and were not counted)

Conclusion

- TL01 five times a week has significantly fewer number of days required to clear psoriasis however, three times a week TL01 requires significantly lower median UVB doses, number of treatments and has fewer Grade 2 erythema.

H.8.7 Different frequencies of narrowband UVB (TL01) – between-patient randomisation

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
H. Cameron, R. S. Dawe, S. Yule, J. Murphy, S. H Ibbotson, J. Ferguson. A randomized, observer-blinded trial of twice vs. three times weekly narrowband ultraviolet B phototherapy for chronic plaque psoriasis. *British Journal of Dermatology.* 147;973-978. 2002	RCT Single-centre (referred to the phototherapy general dermatology clinic), UK Referred May 1998 to December 2000 • Randomised (computer generated random allocation) • Assessor blinded • Sample size	Total N: 113 **Drop-outs (don't complete the study): 29** TL01 twice a week N= 18 4= poor progress 9= poor attendance 2= polymorphic light eruption 1= withdrew as wanted to be in the other group 1= moved	**Inclusion criteria:** Chronic (present or recurring psoriasis for at least 1 year) plaque psoriasis (clinical diagnosis by a Dermatologist) **Exclusion criteria:** Those on immunosuppressive therapy or with a history of skin cancer, patients who had phototherapy/PUVA or systemic psoriasis therapies in the previous 3 months, <16 years of age or were unable to attend reliably. Median age: 41 years (range 17-80)	N=58 **NB-UVB (TL01) twice a week** ---------- **Both arms:** Either a UV5000 Waldmann cubicle or one built by a medical physics department. Both used100W TL01 lamps.	N=55 **NB-UVB (TL01) three times a week**	Treatment was stopped when the patient was clear of psoriasis or in a state of minimal residual activity (MRA) for 4 treatments. Followed up for time to relapse in the following year.	**1° outcome:** number of treatments, dose and time (days) to the clearance of psoriasis **2° and other outcomes:** Psoriasis Severity Scores (SEI) Erythema Remission (psoriasis requiring treatment other than emollients) duration	None stated

Ref ID: CAMERON2002	calculation: 5% level of significance and an 80% completion rate, 44 patients were needed in each group • ITT and competers analysis • There were 3 drop outs for polymorphic light eruption	house 1=treated with 3xweek by error TL01 three times a week N=11 4=poor progress 4= poor attendance 1= polymorphic light eruption 1= wanted to attend 2xweek 1=used self prescribed topical therapy	Sex: 70 male (62%), 43 female (38%) Skin phototypes I-III: no significant difference between the two groups; p=0.27 No other baseline data reported.	MED was done on the upper back skin. MED was the lowest dose that produced a just perceptible erythema in 24 hrs. **Initial dose**: 70% of MED No limit to number of exposures. Treatment days: Mon and Fri. Patients were assessed prior to treatment by an independent assessor. Erythema recorded by nurse phototherapists (not blinded). **Dose escalation:** 20% increase followed by 10% dose increments.			Assessments were made by monthly telephone calls or appointments at the department for relapses.	

				All male patients wore genital protection. All patients wore a face shield unless they had facial psoriasis. Only approved emollients, or scalp, facial and flexural therapies were permitted.				

Effect Size

Outcomes (ITT analysis n=113, Completers analysis (CA) n=84)

Outcomes	**TL01 twice a week (ITT N=58, CA N=40)**	**TL01 three times a week (ITT N=55, CA N=44)**	**Difference (95% CI)**	**p-value**
Number of patients cleared of	40	44	10% fewer (25%	0.21

psoriasis			fewer to 7% more)	
Mean number of days to clearance- CA (range)	88 (48-150)	58 (32-112)		<0.0001
Mean number of treatments to clearance- CA (range)	24.4 (11-41)	23.0 (14-38)		0.15
Mean UVB dose (total dose in multiples of each individual's MEDs) to clearance- CA (range)	125 (17-923)	95 (36-357)		0.062
Relapse (topical therapy other than emollients required) in the year post clearance - CA	Only graphical representation – median = 4.7 months	Only graphical representation median = 3.8 months		0.53
Relapse (further phototherapy or other second line therapy required) in the year post clearance - CA	Only graphical representation median = 21.3 months	Only graphical representation median = 17 months		0.73
Erythema[8] (ITT) Grade 2 Grade 3	 31% 17%	 56% 21%	 25% (7-43%) 4% (-10-19%)	 0.007 0.57

Conclusion

[8] One patient in the twice weekly group had a single episode of blistering erythema (grade 4). It was localized and suggested to be due to a misplacement of genital protection exposing skin not previously exposed.

- Three times a week TL01 requires significantly fewer number of days to clear chronic plaque psoriasis.A higher percentage of grade 2 erythema was found in the three times a week TL01. There were no other significant associations found. A non significant association was demonstrated with TL01 three times a week having a lower total UVB dose than TL01 twice a week.

H.8.8 Home vs out-patient UVB (PLUTO Study)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
M. B. Koek, E. Buskens, H. van Weelden, P. H. Steegmans, C. A. Bruijnzeel-Koomen, and V. Sigurdsson. Home versus outpatient ultraviolet B phototherapy for mild to severe psoriasis: pragmatic multicentre randomised	RCT 'Pragmatic' design: treatments applied under the conditions they usually would be in clinical practice (treatment regimen not imposed) Multi-centre (14 hospital dermatology departments), The Netherlands	Total N: 196 **Drop-outs (don't complete the study):** **Total** lost to follow-up (including those who did not start therapy) Home: 7 (4 did not start therapy)	**Inclusion criteria:** Plaque or guttate psoriasis (mild to severe) clinically eligible for TL01; UVB prescribed by patient's dermatologist; willing to undergo treatment according to randomisation **Exclusion criteria:** age below 18 years; not willing to accept one of the two treatments offered; not able to receive one of the two treatments offered (e.g. lack of space at home/living too far from hospital etc.); analphabetism (unable to read the patient information and the questionnaires, unable to provide written answers and written informed consent); lack of command of the Dutch language; not in possession of a telephone. Expected non-compliance:	N=98 **TL01 home phototherapy unit, 3 or 4 times a week (every other day)** (Waldmann UV 100) Prescribed in units of time (patients given Tx schedule) Patients given 30-60 min training in use of the unit	N=98 **TL01 hospital phototherapy unit, 2 or 3 times a week** Administered according to local hospital's own schedule prescribed in either dose or unit of time Dose	Tx (mean 11.4 and 14.1 weeks for home and hospital, respectively) + 1 year in first 105 recruited	**1° outcome:** PASI50, 50% improvement in SAPASI **2° and other outcomes:** % reduction in median PASI or SAPASI; PASI75, SAPASI75; PASI90; SAPASI90; short-term side effects; SF-36, PDI, EQ-5D	Netherlands Organisation for Health Research and Development

<table>
<tr>
<td>controlled non-inferiority trial (PLUTO study). Br.Med.J. 338:b1542, 2009.

Ref ID: KOEK2009

M. B. Koek, E. Buskens, P. H. Steegmans, H. Weelden, C. A. Bruijnzeel-Koomen, and V. Sigurdsson. UVB phototherapy in an outpatient setting or at home: a pragmatic randomised single-</td>
<td>2002-2005

• Randomised (computer generated list – minimisation method considering recruiting hospital and previous UV therapy)
• No washout period (starting out-patient phototherapy while waiting for home unit was permitted)
• Assessor blinded
• Allocation concealment (central co-ordination centre)
• Sample size calculation based on</td>
<td>Hospital: 11 (3 did not start therapy)

Protocol violation:

5 patients switched therapy (4 from hospital to home)

No difference in severity of psoriasis at baseline between patients who did and did not complete</td>
<td>lack of understanding of what the study/treatment is about, and its potential consequences.

Medical contraindications: Malignancy of the skin in the past/at present; known UVB-allergy or chronic polymorphic photodermatosis; use (at time of inclusion) of medication with known phototoxic or photoallergic properties; use (at time of inclusion) of systemic antipsoriatic medication (ciclosporin, methotrexate, neotigason, fumaric acid); history of exposure to ionising radiation.

<table>
<tr><th>Mean baseline</th><th>Home (n=98)</th><th>Hospital (n=98)</th></tr>
<tr><td>Mean age (SE)</td><td>41.2 (1.38)</td><td>45.0 (1.37)</td></tr>
<tr><td>M/F%</td><td>67</td><td>67</td></tr>
<tr><td>Mean duration of psoriasis ±SE</td><td>16.1 (1.37)</td><td>16.0 (1.36)</td></tr>
</table>
</td>
<td>No MED calculated

BOTH ARMS: no exclusion on grounds of any concomitant treatment initiated after inclusion

Adjuvant topical therapy allowed

Cut-off of 46 Tx to establish effectiveness</td>
<td>determined by minimal erythematic dose (MED) only if standard practice for hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
</table>

blind trial designed to settle the discussion. The PLUTO study. *BMC Med.Res.Meth.* 6:39, 2006. Ref ID: KOEK2006	80% power to detect change of -15% in proportion of patients(2 groups of 90 patients required); 50 per group was considered sufficient for cumulative costs • Available case analysis • Dropouts due to AEs: 0		(years)					
			SAPASI, mean (SE)	7.2 (0.38)	7.3 (0.32)			
			PASI, mean (SE)	9.7 (0.71)	8.6 (0.56)			
			No (%) with experience of phototherapy	50 (51)	50 (51)			

Effect Size

Outcomes (ITT analysis n=196)

Variables, % (n)	Home phototherapy	Outpatient phototherapy	Difference (95% CI)
Effectiveness			

SAPASI 50, 75, and 90*:	(n=94)	(n=91)	—
SAPASI 50	81.9 (77)	79.1 (72)	2.8 (−8.6 to 14.2)
SAPASI 75	69.1 (65)	59.3 (54)	9.8 (−4.0 to 23.6)
SAPASI 90	43.6 (41)	29.7 (27)	13.9 (0.002 to 27.8)
PASI 50, 75, and 90†:	(n=91)	(n=84)	—
PASI 50	70.3 (64)	72.6 (61)	−2.3 (−15.7 to 11.1)
PASI 75	40.7 (37)	41.7 (35)	−1.0 (−15.6 to 13.6)
PASI 90	19.8 (18)	19.0 (16)	0.8 (−10.9 to 12.5)
Safety			
Irradiations:	(n=98)	(n=98)	—
Mean No of irradiations	34.4	28.6	5.8 (2.7 to 9.0)
Mean cumulative dose (J/cm^2):	(n=85)	(n=68)	—
At 23 irradiations	21.2	26.9	−5.7 (−10.3 to −1.1)
	(n=91)	(n=93)	
At end of therapy	51.5	46.1	5.4 (−5.2 to 16.0)
Proportion of side effects per irradiation (%):	(n=93)	(n=92)	—
Severe erythema	5.5	3.6	1.9 (−1.1 to 4.9)
Blistering	0.3	0.6	−0.3 (−0.9 to 0.3)

Burning sensation	7.1	10.0	−2.9 (−7.1 to 1.2)
Mild erythema	28.8	28.6	0.3 (−7.4 to 8.0)
Use of adjuvant drugs, % (n)			
During waiting time (between inclusion and Tx start):	(n=94)	(n=95)	—
Topical steroids	25.5 (24)	6.3 (6)	19.2 (8.8 to 29.6)
Vitamin D derivatives	18.1 (17)	6.3 (6)	11.8 (2.5 to 21.1)
During phototherapy:	(n=92)	(n=92)	
Topical steroids	31.5 (29)	52.2 (48)	−20.7 (−35.0 to −6.4)
Vitamin D derivatives	19.6 (18)	40.2 (37)	−20.6 (−33.8 to −7.4)
Duration of therapy			
	(n=93)	(n=95)	—
Mean duration of therapy (weeks)	11.4	14.1	−2.7 (−4.1 to −1.2)
Mean time from inclusion to end of therapy (weeks)	17.2	16.2	1.0 (−0.6 to 2.5)

- Treatment effect (mean decline in SAPASI and PASI scores) was statistically significant in both treatment groups
- Treatment effect (mean decline in SAPASI and PASI scores) was not significantly different between the 2 groups (p>0.3)

Conclusion

- UV B phototherapy at home is equally effective and equally safe as ultraviolet B phototherapy in an outpatient department when applied in a setting that precludes non-prescribed irradiations.
- Treatment at home also led to a lower burden of treatment and greater patients' satisfaction than did ultraviolet B phototherapy in an outpatient setting, despite waiting times sometimes being considerably longer.
- Home ultraviolet B phototherapy is a worthy alternative to standard outpatient ultraviolet B phototherapy for patients with psoriasis.

H.8.9 PUVA: 2- vs 3-times weekly (between patient randomisation)

<table>
<tr><th>Reference</th><th>Study type</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr>
<td>M. El-Mofty, H. El Weshahy, R. Youssef, M. Abdel-Halim, H. Mashaly, and M. El Hawary. A comparative study of different treatment frequencies of psoralen and ultraviolet A in psoriatic patients with darker skin types (randomized-controlled study). Photodermat</td>
<td>RCT

Single-centre (outpatient clinic), Egypt

Recruited May-Nov 2005

• Randomised (computer generated random number tables)
• 4 wk washout period for topicals and systemics
• Blinding of</td>
<td>Total N: 20

Drop-outs (don't complete the study):

2x weekly: 0

3x weekly: 1</td>
<td>Inclusion criteria: Chronic plaque psoriasis

Exclusion criteria: age <12 years; psoriasis extent <30% or >70%; pregnancy or lactation; liver or kidney disease; photosensitive disorders

<table>
<tr><th>Baseline</th><th>Twice weekly (n=10)</th><th>Three times weekly (n=10)</th></tr>
<tr><td>Mean age</td><td colspan="2">41.95±14.17</td></tr>
<tr><td>M/F%</td><td>40/60</td><td>50/50</td></tr>
<tr><td>Skin type</td><td></td><td></td></tr>
<tr><td>III</td><td>3</td><td>3</td></tr>
<tr><td>IV</td><td>6</td><td>6</td></tr>
<tr><td>V</td><td>1</td><td>1</td></tr>
</table>
</td>
<td>N=10

Oral PUVA, 2 times a week (0.7 mg/kg 8-MOP 2 h before irradiation)

Sessions 2-3 days apart

Max number of Tx: 24

BOTH ARMS:</td>
<td>N=10

Oral PUVA, 3 times a week (0.7 mg/kg 8-MOP 2 h before irradiation)

Sessions 1 day apart

Max number o Tx: 36

----------</td>
<td>Complete clearance or 12 weeks max treatment</td>
<td>1° outcome: PASI

2° outcomes: total number of sessions and total cumulative UV dose

Clinical response graded as

Complete clearance: 100% improvement

Excellent response: 85-100%</td>
<td>None stated</td>
</tr>
</table>

ol.Photoimmunol.Photomed. 24 (1):38-42, 2008. Ref ID: ELMOFTY2008	senior (but not junior) observer • Allocation concealment (not reported) • Sample size calculation (not reported) • ITT analysis not reported • Dropouts due to AEs: unclear		Mean duration of psoriasis ±SD (months): 53.80± 73.36 / 105.10 ±86.45 Extent of lesions (%): 56.00± 11.73 / 51.00± 14.49 PASI: 24.16± 20.07 / 21.61± 15.40	Administered using Waldman PUVA 1000 cabin containing 26 F85/100W lamps (315-400 nm) Initial dosage determined by skin type (1-2 J/cm^2) Increments of 0.5 J/cm2 every other session until mild erythema occurred and then the dose was fixed	**BOTH ARMS:** Adjuvant topical keratolytics used for thick scales Instructed to use sunscreen and wear eye protection during the sessions and for the rest of the day		improvement Very good response: 70-85% improvement Good response: 60-70% improvement Fair response: 50-60% improvement Poor response: <50% improvement	

Effect Size

Outcomes (available case analysis n=19)

Treatment result	2 x a week (n=10)	3 x a week (n=9)

Complete clearance	3	2
Excellent response	6	2
Very good response	1	3
Good response	0	2
Dropped out	0	1

End of Tx outcomes	**2 x a week (n=10)**	**3 x a week (n=9)**	**p-value**
Total UV dose (J/cm^2)	54.57 ± 20.42	99.20 ± 19.48	<0.001
Total sessions	18.70 ± ±5.61	35.33 ± 2.00	<0.001
Final PASI	5.16 ± 6.88	5.88 ± 5.24	0.497
% reduction in PASI	**82.31 ± 18.22**	**66.88 ± 29.31**	**0.356**

Conclusion

- **Reducing PUVA frequency and the cumulative UVA dose does not compromise the efficacy of PUVA, but it may improve its benefit/risk ratio.**

H.8.10 PUVA: 2- vs 3-times weekly (within patient randomisation)

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
M. C. Valbuena, O. Hernandez, M. Rey, G. Sanchez, and L. P. de Quintana. Twice- vs. thrice-weekly MPD PUVA in psoriasis: a randomized-controlled efficacy study. *Photodermatol.Photoimmunol.Photomed*. 23 (4):126-129, 2007. Ref ID: VALBUENA2	RCT – within patient randomised Single-centre (outpatient clinic), Colombia Recruited Feb 2003-Jan 2005 • Randomised (random number tables) • 4 wk washout period for systemics; 2 wk for topicals • Blinded assessor	Total N: 28 **Drop-outs (don't complete the study):** 5	**Inclusion criteria:** Clinical diagnosis of psoriasis; ≥20% BSA involvement (rule of nines) **Exclusion criteria:** age <18 years; pregnancy or lactation; liver or kidney disease; photosensitive disorders; history of adverse reaction to psoralens; systemic treatment within 4 wks of study entry or topicals within 2 wks; phototherapy within 3 months of study entry **Baseline** / **All (n=23)** Mean age: 41.9 ± 15.1 M/F%: 78.3/21.7 **Skin type**	N=28 **Oral PUVA, 2 times a week** (0.6 mg/kg 8-MOP 2 h before irradiation) Sessions on Mondays, and Fridays (half body covered on Wednesdays with protective suit) ----------	N=28 **Oral PUVA, 3 times a week** (0.6 mg/kg 8-MOP 2 h before irradiation) Sessions on Mondays, Wednesdays and Fridays ----------	Up to 25 exposures	**1° outcome:** decrease PASI (excluding assessment of the head) **2° outcomes:** treatments for clearance; cumulative doses	None stated

007	• Allocation concealment (not reported) • Sample size calculation (based on 80% power and 95% confidence = need 44 body halves) • Available case analysis • Dropouts due to AEs: 3		II: 6 III-IV: 17 Ostraceous psoriasis, n (%): 7 (30.4) Mean extent of lesions (%): 48.7 (20-80) PASI: Twice weekly: 31.8±7.3; Thrice weekly: 31.9±7.3; (p=0.758)	**BOTH ARMS:** Administered using Daavlin 305/350 cabinet containing 24 TL-100W lamps Initial dosage determined by MPD Increments of 40%, 20%, 10% or no increment depending on erythema	**BOTH ARMS:** Adjuvant topical treatment only for scalp lesions Wore UV protective goggles			

Effect Size

Outcomes (Available case analysis n=23)

Treatment result	**n**	**2 x a week (n=23) Median (IQR)**	**3 x a week (n=23) Median (IQR)**	**p-value**
% PASI decrease				
Skin type I	6	91.5 (89.9-97.1)	93.2 (91.8-94.0)	0.673

Skin type III-IV	17	93.1 (91-94.9)	95.5 (93.0-96.8)	0.079
Vulgaris type	16	93.6 (92.6-96.4)	95.2 (79.1-99.2)	0.972
Ostraceous subtype	7	90.5 (87.3-91.1)	94.0 (92.8-96.0)	0.043
Total group	*23*	*92.9 (89.9-96.1)*	*94.8 (91.8-96.8)*	*0.179*
Total number of exposures				
Skin type I	6	17.5 (17-25)	25 (25-25)	0.049
Skin type III-IV	17	14 (10-17)	20 (15-25)	0.000
Vulgaris type	16	13 (10-17)	19 (15-24)	0.001
Ostraceous subtype	7	25 (17-25)	25 (25-25)	0.180
Total group	*23*	*15 (11-25)*	*22 (17-25)*	*0.000*
Cumulative dose (J/cm^2)				
Skin type I	6	130.1 (113.0-381.2)	238.9 (167.0-366.3)	0.173
Skin type III-IV	17	144.2 (106.1-238.6)	241.4 (172.3-292.4)	0.003
Vulgaris type	16	120.9 (95.4-146.8)	195.8 (159.5-258.2)	0.000
Ostraceous subtype	7	344.8 (238.6-394.1)	366.3 (257.0-421.9)	1.000
Total group	*23*	*142.5 (106.1-316.0)*	*241.4 (169.7-366.3)*	*0.001*

Adverse events	**2 x a week (n=23)**	**3 x a week (n=23)**

Grade 3 erythema	0	1
Grade 2 erythema	1	1
Mild pruritus	15	16
None	5	1

Conclusion

- **The treatment of psoriasis patients with twice- or thrice-weekly PUVA in this study was equally effective, the number of sessions required and the cumulative doses of UVA were lower with the twice-weekly regimen.**
- **Reducing the frequency of PUVA sessions should enhance adherence and reduce risk of skin cancer and cost of treatment**
- **Ostraceous psoriasis is better treated with the thrice-weekly regimen**

H.8.11 Hand and foot PUVA vs no treatment for palmoplantar pustulosis – within patient randomisation

<table>
<tr><th>Reference</th><th>Study type</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr>
<td>D. Murray, M. F. Corbett, and A. P. Warin. A controlled trial of photochemotherapy for persistent palmoplantar pustulosis. Br.J.Dermatol. 102 (6):659-663, 1980.

Ref ID: MURRAY1980</td>
<td>RCT

Single-centre (referred from outpatient department of St John’s Hospital), UK

• Randomised (unclear method)
• 2 wk washout period for topicals and systemics
• Blinding not reported
• Allocation concealment (not reported)
• Sample size calculation (not</td>
<td>Total N: 22

Drop-outs (don’t complete the study):

0</td>
<td>Inclusion criteria:
Bilaterally symmetrical palmoplantar pustulosis of at least 1 year duration

Exclusion criteria: Not stated

<table>
<tr><th>Mean baseline</th><th>All (n=22)</th></tr>
<tr><td>Mean age (SE)</td><td>Males: 47.8 (2.09)
Females: 52.9 (2.47)</td></tr>
<tr><td>M/F%</td><td>27.3/72.7</td></tr>
<tr><td>Mean age of onset of psoriasis ±SE (years)</td><td>46.1 (2.1)</td></tr>
<tr><td>Mean</td><td>5.3 (0.94)</td></tr>
</table>
</td>
<td>N=22

Oral PUVA, 4 times a week (Mon, Tues, Thurs, Fri) (10 mg 8-MOP tablets taken with food 2 h before irradiation; total dose related to body weight e.g., 30-50 kg = 20 mg; 80-90 kg = 50 mg)

Administered using Waldman UVA 200 hand unit containing 14 F8T5/BL tubes (320-400 nm)</td>
<td>N=22

No treatment

Body side covered during irradiation

BOTH ARMS:

Adjuvant emulsifying ointment BP applied equally to both sides at least twice</td>
<td>30 Tx (7.5 weeks)</td>
<td>1° outcome: Visual analogue scale from 0-100 (0= worse; 25= no change; 50 = improved; 75 = much improved; 100 = cleared)</td>
<td>None stated</td>
</tr>
</table>

	reported) • ITT analysis Dropouts due to AEs: 0		duration of psoriasis ±SE (years)		Initial dosage determined by skin type (0.5-2 J/cm^2) Increments of 0.5-1 J/cm2 made at ≥48-h intervals until clinical improvement and then maintained (or until 1 h of radiation had been given) End point = 30 Tx	daily Patients seen weekly by a single observer (but similar results obtained by an independent observer using photographs)			
			Hands only affected	2					
			Feet only affected	13					
			Feet and hands affected	7					

Effect Size

Outcomes (ITT analysis n=22)

Treatment result	Treated side (n=22)	Untreated side (n=22)
Cleared	12	0
Much improved	5	0
Improved	5	13

No change	0	6
Worse	0	3

- The treated side did better in every case except one where there was modest and similar improvement on both sides ($p<0.001$)
- Mean (SE) Tx dose at clearing: soles = 12 ± 1.20 J/cm^2; palms 10.5 ± 1.44 J/cm^2
- Mean Tx to clear: 26 (range: 18-30)

Duration of remission (number clear and off Tx; note this was after gradual reduction in Tx frequency until it could be stopped)

Duration	**PUVA**	**Untreated**
1 month	1	0
2 months	3	0
6 months	1	0
10 months	1	0

Adverse events

Effect	**PUVA**	**Untreated**
Burn	1	0
Nausea	4	0
Ankle swelling	4	0
Brief non-purulent conjunctivitis	6	0

Conclusion

- **Oral PUVA is effective in clearing palmoplantar pustlosis, but at least 20 treatments may be required (more than for chronic plaque psoriasis)**

<table>
<tr><th>Reference</th><th>Study type</th><th>Number of patients</th><th>Patient characteristics</th><th>Intervention</th><th>Comparison</th><th>Length of follow-up</th><th>Outcome measures</th><th>Source of funding</th></tr>
<tr>
<td>K. Rosen, H. Mobacken, and G. Swanbeck. PUVA, etretinate, and PUVA-etretinate therapy for pustulosis palmoplantaris. A placebo-controlled comparative trial. Arch.Dermatol. 123 (7):885-889, 1987.

Ref ID: ROSEN1987</td>
<td>RCT

Single-centre, Sweden

• Randomised (treatment side according to date of birth)
• 4 wk washout period for topicals and systemics
• Blinding of second assessor
• Allocation concealment (not reported)
• Sample size calculation (not reported)
• Available case analysis</td>
<td>N: 14

Drop-outs (don't complete the study):

2 (1 psoralen reaction; 1 logistical); both with feet to be treated</td>
<td>Inclusion criteria:
Bilaterally symmetrical palmoplantar pustulosis with lesions of comparable severity and morphology on each body side; of at least 6 months duration; previous treatment without satisfactory response; no topical or systemic treatment for PPP for 4 weeks before trial start (except emollients)

Exclusion criteria:
pregnancy; liver or kidney disease; hypertriglyceridemia; alcohol abuse; inability to co-operate/follow instructions

<table>
<tr><th>Mean baseline</th><th>All (n=14)</th></tr>
<tr><td>Mean age (range)</td><td>56 (39-71)</td></tr>
<tr><td>M/F%</td><td>21.4/78.6</td></tr>
</table>
</td>
<td>N=14

Oral PUVA, 3 times a week (Mon, Tues, Thurs, Fri) (0.6 mg/kg 8-MOP tablets taken 1.5 h before irradiation)

Administered using Waldmann PUVA 180+200 unit (200 U placed behind the feet)

Initial dosage 20 kJ/m^2

Increments of 20</td>
<td>N=14

No treatment

BOTH ARMS:

Adjuvant therapy not mentioned

Patients seen every 3 weeks during TX by a single observer observer (but similar</td>
<td>12 weeks max treatment</td>
<td>1° outcome:
Global severity evaluation by physician (cleared = no desquamation or pustulation; much improved = some residual desquamation, pustulation and infiltration; somewhat improved = substantial/easily recognised improvement; unchanged/worse)

Assessment of desquamation, pustlation, erythema, infiltration on a 0 = none to 3 = severe scale</td>
<td>None stated – drugs provided by AB Draco and AB Hoffmann-La Roche</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td>• Dropouts due to AEs: 1</td>
<td></td>
<td>
<table>
<tr><td>Mean duration of psoriasis (years; range)</td><td>7 (0.5-22)</td></tr>
<tr><td>Mean (SE) combined severity score</td><td>Treated side:
9.2 ± 0.5
Untreated side
9.2 ± 0.4</td></tr>
<tr><td>Feet treated</td><td>11</td></tr>
<tr><td>Hands treated</td><td>3</td></tr>
<tr><td>Psoriasis</td><td>5</td></tr>
<tr><td>Previous PUVA</td><td>6</td></tr>
<tr><td>Previous etretinate</td><td>3</td></tr>
</table>
</td>
<td>kJ/m^2 made at each treatment (5 kJ/m^2 increments between 40 and 60 kJ/m^2) to a max of 150 kJ/m^2

No increment if erythema, edema or severe itch occurred

Instructed to wear UVA protective glasses during day of Tx

End point = clearance or max 12 wks

Note: treated *either* hand *or* foot (foot if most severely affected and hand if lesions here caused</td>
<td>results obtained by an independent /blinded observer using photographs)</td>
<td></td>
<td></td>
<td></td>
</tr>
</table>

				most distress)				

Effect Size

Outcomes (ITT analysis n=22)

Treatment result	**Treated side (n=12)**	**Untreated side (n=12)**
Cleared	3	0
Much improved	6	2
Somewhat improved	1	2
No change/worse	2	8
Mean combined severity score at end of Tx	*4.8*	*8.0*

- Of the 3 who cleared 2 were hand PUVA and 1 was foot PUVA; all **relapsed** after ~1 month

Treatment duration for PUVA side

	Total	**At clearance**
Mean (range) number of sessions	29 (16-40)	24 (16-29)
Mean (range) duration of Tx (days)	83 (43-135)	65 (43-86)
Mean (range) total UV dose	1990 (1140-3630)	1990 (1170-2500)

Mean (range) max UV dose (kJ/m^2)	115 (7-150)	130 (120-140)

Adverse events

Effect	**PUVA**	**Untreated**
Symptomatic erythema	4	0
Nausea	3	0
Ankle swelling	1	0
Dermatitis	1	0
Polymorphic light eruption	1	0

Conclusion

- **The choice of treatment for PPP should be individualised according to disease severity and medical background**
- **There is a high relapse rate and patients should be monitored for potential long-term risks**

H.8.12 Hand and foot PUVA vs NBUVB for palmoplantar pustulosis – within patient randomisation

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
E. Sezer, A. H. Erbil, Z. Kurumlu, H. B. Tastan, and I. Etikan. Comparison of the efficacy of local narrowband ultraviolet B (NB-UVB) phototherapy versus psoralen plus ultraviolet A (PUVA) paint for palmoplantar psoriasis. *J.Dermatol.* 34 (7):435-440, 2007. Ref ID:	RCT – within patient (right/left) Single-centre, Turkey • Randomised (computer-based programme) • 2 wk washout period for topicals and 4 wk for systemics • Assessor blinded • Allocation concealment (not reported) • Sample size calculation (not reported) • No ITT analysis	Total N: 25 **Drop-outs (don't complete the study):** **4** 1 = phototoxic reaction to 8-MOP 3 = non-compliance	**Inclusion criteria:** Biopsy-diagnosed PPP of >6 months duration in which conventional therapies (other than phototherapy) proved ineffective **Exclusion criteria:** topical treatment with corticosteroids within 2 weeks or systemic treatment with immunosuppressants and retinoids within the last 4 weeks, unilateral disease, pregnancy, inability to meet follow-up consultations **Mean baseline** / **All (n=25)** Age (range) / 19-75	N=25 **Local NBUVB 3-times a week** Administered using local NB-UVB unit fitted with TL01 bulbs Initial dosage (0.15 J/cm^2) Increments of 20% made at each session until a final dose of 2 J/cm^2 reached	N=25 **PUVA paint 3-times a week** Administered using local UVA unit Initial dosage (1.0 J/cm^2) Increments of 0.5 J/cm^2 made at every second session until a final dose of 7.5 J/cm^2 reached	9 weeks Tx +10 wk follow-up of completers	**1° outcome:** Severity index scores based on separate scores (0, absent; 1, slight; 2, moderate; 3, marked; 4, very marked) of erythema, scaling, pustulation and infiltration for palms and soles (complete clearance = SI of 0; marked clinical improvement = reduction of 70% or more from baseline)	None stated

SEZER2007	• Dropouts due to AEs: 1 (PUVA)		<table><tr><td></td><td>years</td></tr><tr><td>M/F%</td><td>56/44</td></tr><tr><td>Mean duration of PPP (range), years</td><td>5.3 (0.94)</td></tr></table>		Hand and/or foot painted with 1% 8-MOP in hydrophilic water/oil emulsion 15 min before UVA exposure (patiets were advised to wash treated sides after the session) ---------- **BOTH ARMS:** Only topical emollients permitted between treatment sessions; eye shielding employed during irradiation		**2° outcome:** Relapse at 10 weeks (severe = >70% pre-treatment scores; moderate = 30-70% pre-treatment scores; mild = <30% pre-treatment scores) Clinical assessment every 3 weeks by blinded assessor	

Effect Size

Outcomes (available case analysis n=21)

Treatment result (n)	NBUVB (n=21)	PVUA (n=21)
Cleared	0	5
Marked clinical improvement	9	15
Mean cumulative dose (J/cm^2)	34.9	111.5

Relapse at 10 weeks

Relapse	NBUVB (n=21)	PUVA (n=21)
Severe	2	1
Moderate	8	3
Mild	2	3
No relapse	9	14

Adverse events

Effect	NBUVB	PUVA

Phototoxic reaction	0	1
Palmar hyperpigmentation	0	11

Conclusion

- **Although some clinical improvement was observed with local NBUVB, the results were better with local PUVA.**