H.7 Topicals: high impact and difficult to treat sites

H.7.1 VITAMIN D OR VITAMIN D ANALOGUE + POTENT CORTICOSTEROID VS MONOTHERAPIES/PLACEBO

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
G. B. Jemec, C. Ganslandt, J. P. Ortonne, Y. Poulin, A. D. Burden, P. de Unamuno, B. Berne, A. Figueiredo, and J. Austad. A new scalp formulation of calcipotriene plus betamethasone compared with its active ingredients and the	RCT (4-arm) Multicentre (international) SCALP PSORIASIS • **Randomised** Computer-generated. Subjects were randomised in a ratio of 4:4:2:1 • **Washout period**: see exclusion criteria	Total N: **1505** **Drop-outs (don't complete the study): n= 77** **Reasons** Adverse events (n = 8 in combined group, n = 9 betamethasone group; n=20 in calcipotriene group; n=7 in vehicle group) Lack of efficacy (n = 2 in combined group, n = 9 betamethason	**Inclusion criteria:** aged > 18years; scalp psoriasis involving >10% of the scalp surface area; amenable to topical treatment with a maximum of 100 g medication/wk. clinical signs or previous diagnosis of psoriasis vulgaris on trunk and/or limbs. Investigator assessment of clinical signs moderate on at least one sign and other signs at least slight. **Mild to very severe** disease according to investigator's global assessment. **Exclusion criteria:** PUVA or grenz ray therapy within 4 wks before randomisation; UVB therapy within 2 wks before randomisation; systemic biologic therapies with possible effect on scalp psoriasis within 6 months before randomisation; other systemic therapies with possible effect on scalp psoriasis within 4 weeks before randomisation; any topical treatment	Calcipotriene 50 µg/g plus betamethasone 0.5 mg/g (N=541) Betamethasone 0.5 mg/g (N=556) Calcipotriene 50 µg/g (N=272) All in the same vehicle	Vehicle alone (N=136) **Formulation**: scalp gel **Frequency:** once daily --- **BOTH ARMS:** study treatment	Treated for 8 weeks	**1° outcome:** Proportion with absence of disease or very mild disease according to static Investigators Global Assessment **2° and other outcomes:**	LEO Pharma

vehicle in the treatment of scalp psoriasis: a randomized, double-blind, controlled trial. J.Am.Acad. Dermatol. 59 (3):455-463, 2008. Ref ID: JEMEC2008	• **Double blind** – adequately described • **Allocation concealment**. Unclear (pre-planned computer-generated sequence) • **Sample size calculation**. Yes. 90% power and a two-sided 5% significance level (N= 540m 540, 270 and 135 in each group). • **ITT analysis** Yes for efficacy, but not AEs.	e group; n=19 in calcipotriene group; n=16 in vehicle group) Exclusion criteria (n = 3 in combined group, n = 3 betamethasone group; n=2 in calcipotriene group; n=3 in vehicle group) Other (n = 49 in combined group, n = 33 betamethasone group; n=25 in calcipotriene group; n=10 in vehicle group)	of the scalp (except medicated shampoos and emollients) within 2 wks before randomisation; topical treatment of face, trunk or limbs with very potent corticosteroids within 2 wks before randomisation, planned initiation or changes to concomitant medication that could affect scalp psoriasis, planned exposure to the sun, current diagnosis of erythrodermic, exfoliative or pustular psoriasis, presence of viral lesions, fungal or bacterial skin infections, parasitic infections or atrophic skin on the scalp, known or suspected anomaly of calcium homeostasis associated with clinically significant hypercalcaemia, severe renal insufficiency or severe hepatic disorders. **Note:** Patients who were using or recently used biologics were not eligible as these required a washout of >1 month	**Formulation**: scalp gel **Frequency:** once daily **Amount of medication used**: The average weight of study medication used for the entire study period was 139.1 g for the two-compound scalp formulation group, 159.5g for the betamethasone dipropionate group, 155.4 g for the	s applied topically to affected areas of scalp once daily		IAGI (worse to cleared); Adverse events, serum calcium and serum albumin; compliance	

	• **Drop-outs/withdrawals** Combination: 61 (11.3%) Betamethasone: 47 (8.5%) Calcipotriene: 57 (21.0%) Vehicle: 30 (22.1%)			calcipotriene group, and 176.0 g for the vehicle group. The average weight of the study medication used per week was approximately 17 to 22 g/week.				

Demographics

Mean baseline	**Calcipotriene + betamethasone** **N = 541**	**Betamethasone N = 556**	**Calcipotriene** **N = 272**	**Vehicle** **N = 136**
Age, years (mean±SD)	47.9±15.4	49.5±15.9	50.1±16.6	49.6±15.8
Gender M/F	47.9/52.1	41.9/58.1	44.5/55.5	44.9/55.1
Race (Caucasian%)	95.7%	96.8%	97.4%	94.9%

Duration of scalp psoriasis, years (mean±SD)	15.4±13.5	17.4±13.5	16.7±14.0	16.3±13.1
TSS (mean ± SD)	6.7±1.9	6.9±1.8	6.8±1.8	7.0±1.9
Investigators global assessment of disease severity (%)				
Mild	8.7	4.5	5.9	7.4
Moderate	56.2	57.0	57.4	50.7
Severe	28.8	32.9	32.0	36.0
Very severe	6.3	5.6	4.8	5.9

Effect Size

Outcomes

Efficacy & time to effect

Patients achieving absent or very mild disease on IAGI (%)	**Calcipotriene + betamethasone N = 541**	**Betamethasone N = 556**	**Calcipotriene N = 272**	**Vehicle N = 136**
Week 2	311 (57.5%)	262 (47.1%)	51 (18.8%)	16 (11.6%)

Week 4	362 (66.9%)	304 (54.7%)	64 (23.5%)	20 (14.7%)
Week 8 (primary outcome)	385 (71.2%)	356 (64.0%)	100 (36.8%)	31 (22.8%)

Patients overall assessment of treatment response at week 8 (name of scale not reported)

	Calcipotriene + betamethasone N = 541	**Betamethasone N = 556**	**Calcipotriene N = 272**	**Vehicle N = 136**
Proportion of patients who rated their scalp psoriasis as 'cleared' or 'almost clear' at week 8 (PAGI)	371 (68.6%)	348 (62.5%)	104 (38.3%)	28 (20.7%)

The two compound scalp formulation was significantly more effective than calcipotriene (OR 3.54; 99.3% CI, 2.28 TO 5.50; P<0.0001) and the vehicle alone (OR 8.45; 99.3% CI, 4.49 to 15.91; p<0.0001). The difference versus betamethasone dipropionate was not statistically significant (OR 1.38; 99.3% CI, 0.95 to 1.99; p=0.2)

Withdrawals

	Calcipotriene + betamethasone N = 541	**Betamethasone N = 556**	**Calcipotriene N = 272**	**Vehicle N = 136**

Total	61	47	57	30
Adverse events	8	6	20	7
Treatment failure	2	9	19	16

Compliance

	Calcipotriene + betamethasone N = 541	**Betamethasone N = 556**	**Calcipotriene N = 272**	**Vehicle N = 134**
Study medication used as instructed	37.9%	47.5%	42.6%	49.3%
Absence of disease recorded so allowed to miss applications	33.5%	25.9%	11.0%	4.4%

Summary

- Calcipotriene plus betamethasone dipropionate scalp formulation was more effective than either of the individual components or the vehicle alone

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
P. C. van de Kerkhof, V. Hoffmann, A. Anstey, L. Barnes, C. Bolduc, K. Reich, S. Saari, S. Segaert, and L. Vaillant. A new scalp formulation of calcipotriol plus betamethasone dipropionate compared with each of its active ingredients in the same vehicle for the treatment of scalp psoriasis: a	RCT Multicentre International Parallel group (3 arm) SCALP PSORIASIS • **Setting:** out-patient • **Randomised** Computer-generated (ratio 2:2:1). • **Washout period**: 2 wk to 1 month depending on previous	Total N: **1418** **Drop-outs (don't complete the study):** **TCF:** 48 (8.5%) **Betamethasone:** 66 (11.7%) **Calcipotriol:** 38 (13.3%)	**Inclusion criteria:** aged ≥ 18 years; **mild-to-very severe** scalp psoriasis on PGA (affecting at least 10% of scalp area) amenable to topical treatment with a max of 100 g medication per week. Clinical signs or previous diagnosis of psoriasis vulgaris on trunk and/or limbs. One or more clinical signs at least moderate and the others at least slight. **Exclusion criteria**: any topical treatment of the scalp (except medicated shampoos and emollients), topical treatment of face, trunk or limbs with very potent corticosteroids or UVB within 2 weeks of randomisation. PUVA or grenz ray therapy within 4 wks before randomisation; systemic biologic therapies with possible effect on scalp psoriasis within 6 months before randomisation; planned initiation or changes to concomitant medication that could affect scalp psoriasis, planned exposure to the sun, current diagnosis of erythrodermic, exfoliative or pustular psoriasis, presence of viral lesions, fungal or bacterial skin	Calcipotriol 50 µg/g plus betamethasone 0.5 mg/g (Xamiol) (N=568) **Formulation**: scalp gel **Frequency:** once	Betamethasone 0.5 mg/g (N=563) Cacipotriol 50 µg/g (N=286) **Formulation**: same vehicle as TCF **Frequency:** once daily ---------- **BOTH**	Treated for up to 8 weeks	IGA (clear/very mild) Patient's global assessment (clear or nearly clear) Withdrawals	Leo Pharma

randomized, double-blind, controlled trial. Br.J.Dermatol. 160 (1):170-176, 2009. Ref ID: VANDEKERKHOF2009	therapy • **Double blind** – states double blind but no details • **Allocation concealment**. Unclear • **Sample size calculation**. No stated • **ITT analysis** Yes (LOCF).		infections, parasitic infections or atrophic skin on the scalp, known or suspected anomaly of calcium homeostasis associated with clinically significant hypercalcaemia, severe renal insufficiency or severe hepatic disorders. **Note:** the majority of patients had moderate-to-severe disease	daily	**ARMS:** patients with 'absence of disease' on PGA could stop treatment at investigators discretion but were required to attend visits (could restart treatment if required)			

Demographics

Mean baseline	**TCF** **N = 568**	**Betamethasone** **N = 563**	**Calcipotriol** **N=286**
Age, years (mean±SD)	48.5±16.4	47.9±16.4	48.7±16.2
Gender M/F%	41.9/58.1	46.2/53.8	47.9/52.1
Race – white, n (%)	559 (98.4%)	545 (96.8%)	274 (95.8)

TSS 0-15 (mean)	6.8±1.9	6.9±1.8	6.8±1.8

Effect Size

Outcomes

Mean weight of study medication used: 163.8 g for TCF; 177.2 g for betamethasone; 192.3 g for calcipotriol

Efficacy & time-to-effect

Investigators assessment

IGA week 8	**TCF** **N = 567**	**Betamethasone** **N = 562**	**Calcipotriol** **N=286**
Absence of disease (discontinued applications)	149 (26.2%)	123 (21.8%)	34 (11.9%)
Very mild	197 (34.7%)	193 (34.3%)	80 (28.0%)

IGA (absent/very mild)	**TCF**	**Betamethasone**	**Calcipotriol**

	N = 567	**N = 562**	**N=286**
Week 2	278 (49.0%)	216 (38.4%)	45 (15.7%)
Week 4	311 (54.9%)	287 (51.1%)	74 (25.9%)
Week 8 (primary outcome)	388 (68.4%)	343 (61.0%)	124 (43.4%)

Patients assessment

Week 8	**TCF** **N = 567**	**Betamethasone** **N = 562**	**Calcipotriol** **N=286**
Clear/nearly clear	395 (69.6%)	337 (59.9%)	128 (44.7%)

Withdrawals

	TCF **N = 568**	**Betamethasone** **N = 563**	**Calcipotriol** **N=286**
Withdrawal due to adverse events	4	7	8
Withdrawal due to lack of efficacy	7	9	8

Author's conclusion

- The two-compound scalp formulation was well tolerated and more effective in the treatment of scalp psoriasis than either of its individual components in the same vehicle

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
C. Buckley, V. Hoffmann, J. Shapiro, S. Saari, F. Cambazard, and M. Milsgaard. Calcipotriol plus betamethasone dipropionate scalp formulation is effective and well tolerated in the treatment of scalp	RCT (2-arm) Multicentre (international) SCALP PSORIASIS • **Randomised** Unclear • **Washout period**: see exclusion criteria • **Double blind**	Total N: **218**	**Inclusion criteria:** aged ≥18years; scalp psoriasis involving >10% of the scalp surface area; amenable to topical treatment with a maximum of 100 g medication/wk. **Mild to very severe** disease according to investigator's global assessment. **Exclusion criteria:** PUVA therapy within 4 wks before randomisation; UVB or grenz ray therapy or topical treatment of scalp psoriasis or other relevant skin disorder within 2 wks before randomisation; systemic therapies with possible effect on scalp psoriasis within 4 weeks before randomisation; erythrodermic or pustular	**N=108** Calcipotriene 50 µg/g plus betamethasone dipropionate 0.5 mg/g **Formulation**: scalp gel **Frequency:** once daily **Amount of**	**N=110** Betamethasone dipropionate 0.5 mg/g **Formulation**: scalp gel (same vehicle) **Frequency:** once daily	Treated for up to 8 weeks (mean duration 6.1 weeks in combined and 6.8 weeks for mono-therapy)	IAGI (worse to cleared); treatment success measured by patient Adverse events and adverse drug reactions; compliance	LEO Pharma

psoriasis: a phase II study. Dermatology 217 (2):107-113, 2008. Ref ID: BUCKLEY2008	– not described • **Allocation concealment**. Unclear • **Sample size calculation**. No • **ITT analysis** Yes for efficacy, but not AEs. Primary outcome assessed ITT and PP • **Drop-outs/withdrawals** Combination: 47 (43.5%) Betamethasone: 33 (30.0%)		psoriasis, known or suspected severe renal insufficiency or severe hepatic disorders.	**medication used:** The average weight of medication used was similar between the groups (17.3 g/week for the two compound group and 17.1g/week for the betamethasone group) and remained fairly constant throughout the trial.	---------- **BOTH ARMS:** study treatments applied topically to affected areas of scalp once daily in the same vehicle			

	Note: of these the number withdrawing according to the protocol owing to 'absence of disease' were Combination: 33 (30.6%) Betamethasone: 24 (21.8%) So the unplanned withdrawals were Combination: 14 (12.9%) Betamethasone: 9 (8.2%)							

Demographics

Mean baseline	**Calcipotriene + betamethasone** **N = 108**	**Betamethasone** **N = 110**
Age, years	48.4±16.5	48.4±14.4

(mean±SD)		
Gender M/F	43.5/56.5	46.4/53.6
Race (Caucasian%)	97.2%	98.2%
Duration of scalp psoriasis, years (mean±SD)	16.0±15.5	13.2±12.0
TSS (mean ± SD)	6.79±1.53	6.81±1.63

Effect Size

Outcomes

Efficacy

	Calcipotriol + betamethasone N = 108	**Betamethasone N = 110**	Mean difference	95% CI	p-value
Treatment success (at least marked improvement on PAGI)	100 (92.5%)	91 (82.6%)	9.9%	1.3-18.7%	0.027

- The distribution of IGA at the end of treatment was in favour of the two compound scalp formulation, with 8.8% more patients achieving controlled disease in the two compound group than in betamethasone dipropionate group (95% CI: -2.0, 19.5; p=0.11)

Time to effect

- Both products showed a rapid onset of action, with an effect registered by change in TSS after 1 week of treatment
- Based on absolute change in TSS maximal effect was not achieved by the trial endpoint with either treatment

Withdrawals

	Calcipotriol + betamethasone **N = 108**	**Betamethasone** **N = 110**
Total	47	33
Total (not including due to absence of disease)	14	9
Adverse events	1	2
Treatment failure	0	2

Compliance

	Calcipotriene + betamethasone **N = 107**	**Betamethasone** **N = 110**

Fully compliant or missed <20% of applications	93 (86.1%)	103 (93.6%)

Authors conclusion

- The two-compound scalp formulation provided clinically significant improvements after 2 weeks and remained throughout the study period.
- The two-compound scalp formulation was well-tolerated and compliance was high.
- Calcipotriene plus betamethasone dipropionate scalp formulation was superior to betamethasone dipropionate alone

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Kragballe K et al. Efficacy and safety of calcipotriol plus betamethasone dipropionate scalp formulation compared with calcipotriol scalp solution in the treatment of scalp psoriasis: a randomized controlled trial. Br J Dermatol 2009; 161:	RCT 17 centres in Belgium, Canada, Denmark, France and Sweden. SCALP PSORIASIS • **Setting:** out-patient • **Randomised** Assigned an exclusive randomisation code in ascending order (generation of code not stated); randomised 2:1	N= 312 **Drop-outs (don't complete the study): 40 (12.8%)** Group 1: 17 (8.2%) Group 2: 23 (21.9%) **Reasons:** not stated for all	**Inclusion criteria:** Scalp psoriasis amenable to topical treatment; 18 years old or over; clinical signs or prior diagnosis of psoriasis vulgaris on trunk and/or limbs; 10% or more of total scalp area involved; clinical signs (redness, thickness, scaliness) of at least "moderate" on one sign and at least "slight" on each of the other 2 signs; investigator's global assessment of disease **at least "moderate".** **Exclusion criteria:** Psoralen and ultraviolet A or Grenz ray therapy within 4 weeks; ultraviolet B within 2 weeks; biological therapies that could affect scalp psoriasis within 6 months; other systemic therapy that could affect scalp psoriasis within 4 weeks; topical treatment on the scalp within 2 weeks; or very potent (WHO group IV) corticosteroids elsewhere on body within 2 weeks; unstable forms of psoriasis or other skin diseases confounding psoriasis	Group 1: 2-compound scalp formulation of calcipotriol 50 µg/g + betamethasone 0.5mg/g; maximum 100g per week (Xamiol) **Formulation**: scalp gel **Frequency:** once daily **Concomitant therapy:**	Group 2: Calcipotriol scalp solution twice daily 60ml (50µg/ml) per week (Dovonex) **Formulation**: scalp solution **Frequency:** twice daily **Concomitant therapy:** No other topical treatments or emollients were allowed	Phase 1 = 8 weeks of treatment; then phase 2 = observation phase (entered if "clear" or "minimal" disease) of further 8 weeks	**Primary outcome:** clear or minimal disease at wk 8 on IGA scale: clear, minimal, mild, moderate, severe, very severe). **Secondary outcomes:** *Relapse* = recurrence of at least moderate disease according to IGA.	LEO Pharma

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KRAGBALL
E2009</td>
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Washout period: 2-4 weeks

• Single blind (investigator)

• Allocation concealment – not stated

• Sample size calculation Estimated sample size 160-185 patients in group 1 and 80-93 in group 2 for 90% power

• ITT analysis Yes (LOCF)

• Drop-outs/withdrawals

312 patients randomised (207
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assessment; skin infections, infestations or atrophy or the scalp; abnormalities in calcium homeostasis; severe renal or hepatic disorders; concomitant use of medications with a possible effects on scalp psoriasis; pregnant or breastfeeding.
<table>
<tr><td></td><td>Group 1</td><td>Group 2</td></tr>
<tr><td>Age (yr) mean (SD) range</td><td>50.8 (15.3) 18-91</td><td>51.4 (15.6) 24-85</td></tr>
<tr><td>Men n (%)</td><td>90 (43.5%)</td><td>44 (41.9%)</td></tr>
<tr><td>Caucasian n (%)</td><td>205 (99.0%)</td><td>104 (99.0%)</td></tr>
<tr><td>Duration of psoriasis (yr)</td><td>18.4 (13.8) 0-62</td><td>19.3 (16.0) 1-70</td></tr>
<tr><td>Investigator’s global assessment
Moderate
Severe
Very severe</td><td>

113 (54.6%)
78 (37.7%)</td><td>

64 (61.0%)
34 (32.4%)</td></tr>
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<td>No other topical treatments or emollients were allowed</td>
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<td>Rebound = 1-category increase in IGA from baseline.

Adverse events</td>
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	group 1 and 105 group 2); 190 + 82 completed treatment phase; 135 + 29 entered observation phase; 115 + 27 completed observation phase								

	1`6 (7.7%)	7 (6.7%)
SF-36 score		
Physical	51.4 (8.4 (22-67)	52.3 (7.8) 30-63
Mental	50.2 (9.4) 22-69	51.0 (8.4) 26-67
Skindex-16 score	51.5 (23.6) 0-100	49.6 (21.0) 2-91

Effect Size

Efficacy & time-to-effect

Treatment phase

	Group 1: 2-compound scalp formulation of calcipotriol + betamethasone	**Group 2: Calcipotriol scalp solution**	**Odds ratio (CI), p value**
Proportion of patients with 'clear' or 'minimal' disease according to IGA at week 2	125/207 (60.4%)	11/105 (10.5%)	-
Proportion of patients with 'clear' or 'minimal' disease according to IGA at week 4	114/207 (55.1%)	19/105 (18.1%)	-
Proportion of patients with 'clear' or 'minimal' disease according to **IGA** at week 8 (primary endpoint)	142/207 (68.6%)	33/105 (31.4%)	OR 5.4, 95% CI 3.1 to 9.4;p<0.001
Proportion of patients with 'clear' or 'very mild	170/207 (82.1%)	36/105 (34.3%)	OR 9.4, 95% CI 4.3 to 20.3;p<0.001

disease according to **patient's** assessment at week 8			
Withdrawals due to AE in treatment phase	2/207 (1.0%)	9/105 (8.6%)	
Skin atrophy	0/207	0/105	
Compliance (missed ≤10% of applications)	170/206 (82.5%)	82/102 (80.4%)	*Note: compliance data not available for all patients*

Time to maximum effect (based on mean TSS):

- Mean TSS plateaux after 2 wks for calcipotriol vs 4 wks for two-compound formulation
- Over the first 2 weeks of treatment , the mean TSS for the two compound formulation decreased more rapidly than for the calcipotriol scalp solution and remained below that of the calcipotriol scalp solution throughout the treatment period to week 8

Observation phase

	Group 1: 2-compound scalp formulation	**Group 2: Calcipotriol scalp solution**	**Odds ratio (CI), p value**
Relapse: number of patients median time to relapse meeting criteria for rebound	 73/135 (54.1%) 35 days 2 (1.5%)	 10/29 (34.5%) 58 days 0	Not calculated (groups not randomised; far fewer entered from group 2)

Authors conclusion

- Once daily 2-compound scalp formulation of calcipotriol + betamethasone significantly more effective than twice daily calcipotriol scalp solution with fewer adverse effects and a low rate of withdrawals for patients with moderate to severe scalp psoriasis, although it is not a cure and relapse may be expected.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Tyring S et al. A calcipotriene / betamethasone dipropriona te two-compound scalp formulatio n in the treatment of scalp psoriasis in Hispanic/ Latino and Black/ African American patients: results of the randomize d, 8-week, double-blind phase	**RCT** **DESIGN** Between patient Patient delivery **ALLOCATION** Random Method of randomisation: computer generated Concealment: unclear **BLINDING** double-blind • **Washout period:** 2 weeks • **Sample size calculation:**	**Total N: 177** **Drop-outs (don't complete the study):** Total = 19 (10.7%): 14 in two-compoun d group and 5 vehicle group excluded for failure to apply medicatio n correctly, no post-baseline data or	INCLUSION CRITERIA Age 18 or above; psoriasis involving at least 10% of the scalp and trunk/limbs; an investigator's global assessment of moderate, severe or very severe scalp psoriasis; participants who self-report their ethnicity as Hispanic or Latino, and their race as Black or African American; females of child-bearing potential must have a negative result for a urine pregnancy test before randomisation and must agree to use an adequate method of contraception during the study. EXCLUSION CRITERIA Erythrodermic, exfoliative or pustular psoriasis; skin infections/diseases; disorders of calcium metabolism; pregnancy/ breastfeeding; concurrent antipsoriatic treatment; chemical treatments of the hair	**n=135** **Calcipotriene / betamethasone diproprionate two-compound scalp formulation** **Formulation:** scalp gel **Class:** vitamin D analogue plus corticosteroid **Frequency:** once daily	**n=42** **Vehicle** **Formulation**: scalp gel **Frequency :** once daily	**Treatment duration:** 8 weeks **Assessments at:** every 2 weeks	Investigator global assessment (6-point scale where 1=absence of disease to 6=very severe disease); Investigator assessment of redness, thickness and scaliness, each on 0-4 scale (0=none to 4=very severe); adverse events; patient's	

of a clinical trial. Int J Dermatol 2010; 49: 1328-1333. **Ref ID: TYRING2010**	reported • **ITT analysis:** yes **Setting:** Outpatients	use of excluded treatments; 7 and 4 provided no data on AEs; 27 (15.3%) withdrew: 19 (14.1%) in two-compound group and 8 (19.0%) in vehicle group Non-compliance: 78.5% of patients applied scalp formulation on at least 90% of days vs. 73.8% in vehicle group	BC: yes Mean age around 45 years (range 18-76) 44% male 99 Hispanic/ Latino (75 in two-compound group and 24 in vehicle group) and 78 Black/ African American (60 in two-compound group and 18 in vehicle group) Mean duration psoriasis around 11 years (range 1-50) Around 80% moderate and 20% severe/very severe scalp psoriasis Mean TSS around 6.3 (range 4-11)	**Amount used:** maximum 40g/week; mean 12.5g/week (range 0.1 to 34.9) in the two-compound group and 11.8g/week (range 0.0 to 28.8) in vehicle group; mean duration of exposure 7.6 weeks (range 0.1-15.6) in two-compound group and 7.4 weeks (0.0 to 14.0) in vehicle group			global assessment (5-point scale where n=clear and 4=severe); compliance (returned medication bottles weighed); TSS ≤1 **Primary efficacy parameter:** proportion of patients with cleared/minimal disease by Investigator global assessment at week 8	

Effect Size

Outcomes

Efficacy

ITT analysis	**Calcipotriene / betamethasone dipropionate two-compound scalp formulation n=135**	**Vehicle n=42**	**Odds ratio (95% CI), p value**
Proportion of patients with cleared/minimal disease by Investigator global assessment at week 8:	97 (71.9%)	17 (40.5%)	3.30 (1.62 to 6.72), p<0.001
Hispanic/ Latino	49 (65.3%) of 75 patients	8 (33.3%) of 24	
Black/ African American	48 (80.0%) of 60 patients	9 (50.0%) of 18	
Cleared/very mild disease by patient's global assessment	84 (62.2%)	15 (35.7%)	2.97 (1.11 to 7.93), p=0.004*

PP analysis	**Calcipotriene / betamethasone dipropionate two-compound scalp formulation n=121**	**Vehicle n=37**
Proportion of patients with cleared/minimal disease by Investigator global assessment at week 8:	97 (80.2%)	16 (43.2%)

* p values <0.01 considered significant for secondary criteria to account for multiplicity

Adverse events/ Withdrawals:

	Calcipotriene / betamethasone dipropionate two-compound scalp formulation n=135	**Vehicle n=42**	**Odds ratio (95% CI), p value**
ADR = adverse events possibly/probably related to treatment (none severe)	9 (7.0%) patients with 11 events	3 (7.9%) pts with 4 events	0.88 (0.23 to 3.44), p=1.00
Constipation	1 (0.8%)	0	
Dizziness	1 (0.8%)	0	
Dry skin	1 (0.8%)	0	
Dysgeusia	0	1 (2.6%)	
Folliculitis	1 (0.8%)	0	
Headache	1 (0.8%)	1 (2.6%)	
Hyperaesthesia	1 (0.8%)	0	
Hyperhidrosis	1 (0.8%)	0	
Hypoesthesia	1 (0.8%)	0	
	2 (1.6%)	1 (2.6%)	

Paraesthesia Skin irritation	1 (0.8%)	1 (2.6%)	
Serious AE unrelated to treatment	1 CVA; 1 nausea (withdrew); 1 nausea, tremor and depression (withdrew)	0	

No clinically significant changes in blood chemistry.

Time-to-effect: week 8 data only

Authors' conclusion

The two-compound calcipotriene / betamethasone dipropionate scalp formulation was safe and effective in the treatment of scalp psoriasis in Hispanic/ Latino and Black/ African American patients.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Luger TA, Cambazard F, Larsen FG, Bourcier M, Gupta G, Clonier F, et al. A Study of the Safety and Efficacy of Calcipotriol and Betamethasone Dipropionate Scalp Formulation in the Long-Term Management of Scalp Psoriasis. Dermatology 2008; Vol. 217, issue 4:321–8.	**RCT** **DESIGN** Between patient Patient delivery **ALLOCATION** Random Method of randomisation: computer generated Concealment: unclear **BLINDING** double-blind • **Washout period:** up to 28 days • **Sample size calculation :** not reported	**Total N: 869** **Drop-outs (don't complete the study):** Total = 267 (30.7%); 92/429 (21.4%) of patients in two compound group and 175/440 (39.8%) in calcipotriol group, p<0.001 Noncomp	INCLUSION CRITERIA Age 18 or over; scalp psoriasis amenable to topical treatment with a maximum of 100g study medication per week; also clinical signs/previous diagnosis of psoriasis on trunk/limbs; psoriasis involving at least 10% of the scalp; an investigator's global assessment of moderate, severe or very severe scalp psoriasis. EXCLUSION CRITERIA Concurrent antipsoriatic treatment; disorders of calcium metabolism BC: yes Mean age around 49 years (range 18-86) 44% male 97% Caucasian Mean duration psoriasis around	**n=429** **Calcipotriol and Betamethasone Dipropionate Scalp Formulation** **Formulation:** Scalp gel **Class:** vitamin D analogue plus corticosteroid **Frequency:** once daily when required	**n=440** **Calcipotriol** **Formulation**: Scalp gel **Frequency:** once daily when required	**Treatment duration:** 52 weeks **Assessments at:** baseline and every 4 weeks	Adverse drug reactions (ADRs); any type of adverse event Investigator or global assessment (6-point scale where 1=absence of disease to 6=very severe disease); patient's assessment (satisfactory or not satisfactory); complianc	LEO Pharma

Ref ID: LUGER2008	• **ITT analysis:** not stated **Setting:** Outpatients	liance: 70.9% of patients in two compound group >90% compliant vs. 58.9% in calcipotriol group	17.5 years (range 1-72 years) Investigator assessment of disease severity: moderate: 55.5%; severe: 37.8%; very severe: 6.7%	**Amount used:** mean weekly weight used 10.6g in two compound group and 12.8g in calcipotriol group; mean weight used over whole study period 470.8g and 440.0g; mean duration treatment 44 weeks and 37 weeks.			e (medication used once or twice daily at all visits, or not used because not needed; weighing returned tubes) **Primary efficacy parameter:** Adverse drug reactions (ADRs); any type of adverse event	

Effect Size

Outcomes

Efficacy

Investigator global assessment: patients with absent/very mild/mild disease – only shown graphically

	Calcipotriol and Betamethasone Dipropionate Scalp Formulation **n=429**	**Calcipotriol** **n=440**	**p value**
median number of visits per patient with satisfactorily controlled disease (absent/very mild/mild disease)	92.3% of assessments	80.0%	p<0.001
Patient assessment satisfactory at every visit	76.2%	50.2%	p<0.001

Time-to-effect: number of patients with absent/very mild/mild disease started at each 4-week assessment displayed graphically but unclear

Adverse events:

No skin atrophy reported.

Withdrawals

	Calcipotriol and Betamethasone Dipropionate Scalp Formulation **n=429**	**Calcipotriol** **n=440**	**p value**
Withdrawal due to unacceptable treatment efficacy	14 (3.3%)	51 (11.6%)	
Withdrawal due to AEs	9 (2.1%)	44 (10.0)	
Death	1 (0.2%)	1 (0.2%)	
Exclusion criteria	5 (1.2%)	15 (3.4%)	
Lost to follow up	26 (6.1%)	29 (6.6%)	
Other reasons (personal/dissatisfaction with cosmetic appeal/unable to attend visits)	24 (5.6%)	47 (10.7%)	
Voluntary	17 (4.0%)	18 (4.1%)	
Total withdrawals (patients could have >1 reason)	92 (21.4%)	175 (39.8%)	p<0.001

Authors' conclusion

The Calcipotriol and Betamethasone Dipropionate Scalp Formulation demonstrated high levels of safety and efficacy in long-term management of scalp psoriasis.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Jemec GBE et al. Significant one week efficacy of a calcipotriol plus betamethasone dipropionate scalp formulation. JEADV 2011; 25: 27-32 **Ref ID: JEMEC2011**	**Pooled data from 2 phase III RCTs** **DESIGN** Between patient Patient delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Double-blind • **Washout period:** 2 weeks • **Sample size calculation** not reported	**Total N: 2920** **Drop-outs (don't complete the study):** Total = 40 (1.4%): 15 two-compound group; 14 betamethasone group; 10 calcipotriol group; 1 vehicle group plus withdrawal due to AEs in first week:	INCLUSION CRITERIA Adults with >10% of the scalp affected by mild to very severe psoriasis; scalp psoriasis amenable to topical treatment with maximum 100g/week; 1 or more clinical signs (redness, thickness or scaliness) with a score of at least 2 (moderate) and a score of at least 1 (slight) for the remaining 2. EXCLUSION CRITERIA Very potent corticosteroids and, in study 1, vitamin D analogues BC: Yes Age: median around 50 years (range: 18 to 97) Gender (%M): around 45% Ethnicity: around 97% Caucasian Severity: around 8% mild; 55% moderate; 31% severe; 6% very severe; mean TSS around 6.8 at baseline	**n=1108** **Calcipotriol 50µg/g and Betamethasone 0.5mg/g as dipropionate** **Formulation:** scalp formulation **Class:** vitamin D analogue plus corticosteroid **Frequency** once daily **Amount used:**	**a) Betamethasone 0.5mg/g as dipropionate: n=1118; b) Calcipotriol 50µg/g: n=558; c) vehicle: n=136** **Formulation**: scalp formulation **Frequency** once daily Study 1: all 4 groups;	**Treatment duration:** 8 weeks **Assessments at:** 1 week and 8 weeks **Follow-up after end of treatment:** none	Investigator global assessment (6-point scale where 1=absence of disease to 6=very severe disease); endpoint absent or very mild disease. Patient's overall assessment of treatment response on a 7-point scale from 1=cleared to	Leo Pharma A/S

	• **ITT analysis:** not stated **Setting:** Outpatients	two-compound group 5 (0.5%); betamethasone group 2 (0.2%); calcipotriol group 13 (2.4%); vehicle group 2 (1.5%)	Duration (median around 12 years): (range: 0 to 72)	mean in first week: 21.6g in two-compound group; 22.9g betamethasone group, 23.4g calcipotriol group and 24.4g in vehicle group	study 2: no vehicle group		7=worse; endpoint cleared or almost clear. **Primary efficacy parameter:** not stated	

Effect Size

Outcomes

<u>Efficacy</u>

At 1 week:

	two-compound group	betamethasone group	calcipotriol group (n=558)	vehicle group (n=136)

	(n=1108)	(n=1118)		
Absent/very mild disease (Investigator global assessment)	331 (30.6%) p<0.001 vs. all other groups	262 (24.1%)	54 (10.0%)	9 (6.9%)
Clear/almost clear (patient assessment)	200 (18.5%) p<0.001 vs. all other groups	148 (13.6%)	22 (4.1%)	5 (3.8%)

Time-to-effect (TCF)

Effect seen at week 1; almost 90% of total response seen by week 2 (64.0% reduction in TSS in two-compound group) with small additional improvement up to week 8 (73.3% reduction in TSS in two-compound group) – data not shown for other groups.

Adverse events Withdrawals:

	two-compound group (n=1108)	betamethasone group (n=1118)	calcipotriol group (n=558)	vehicle group (n=136)
Pruritis	15 (1.4%)	4 (0.4%)	22 (4.0%)	3 (2.2%)
Burning sensation	2 (0.2%)	4 (0.4%)	5 (0.9%)	0
Skin burning sensation	2 (0.2%)	0	1 (0.2%)	0
Skin irritation	1 (0.1%)	1 (0.1%)	6 (1.1%)	1 (0.7%)
Paraesthesia	1 (0.1%)	1 (0.1%)	2 (0.4%)	0
Alopecia	0	3 (0.3%)	1 (0.2%)	0
Psoriasis	0	1 (0.1%)	2 (0.4%)	0

Erythema	0	0	6 (1.1%)	0
Dermatitis contact	0	0	2 (0.4%)	1 (0.7%)
Total number of patients with lesional/perilesional AE	27 (2.5%)	22 (2.0%)	53 (9.7%)	5 (3.7%)
Withdrawal due to AEs	5 (0.5%)	2 (0.2%)	13 (2.4%)	2 (1.5%)

Authors' conclusion

The two-compound group demonstrated efficacy at week 1 with a faster onset of effect than either of the individual components in the same vehicle in the treatment of scalp psoriasis.

H.7.2 VITAMIN D OR VITAMIN D ANALOGUE VS POTENT CORTICOSTEROID

<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>P. Reygagne, U. Mrowietz, J. Decroix, de Waard-van der Spek FB, L. O. Acebes, A. Figueiredo, R. Caputo, M. Poncet, and S. Arsonnaud. Clobetasol propionate shampoo 0.05% and calcipotriol solution 0.005%: a randomized comparison of efficacy and safety in subjects with scalp</td>
<td>RCT

Multicentre

SCALP PSORIASIS

• Randomised
Computer-generated.

• Washout period: not stated

• Single blind – investigator (adequately described)

• Allocation concealment. Unclear</td>
<td>Total N: 151

Drop-outs (don’t complete the study): 14
3 (3.9%) on clobetasol and 11 (14.7%) on calcipotriol

Reasons

7 in calcipotriol group due to AEs

Protocol deviation</td>
<td>Inclusion criteria: aged ≥ 12 years; moderate-to-severe scalp psoriasis (GSS at least 3/5 and affected area at least 2 cm^2 of scalp.

Exclusion criteria: Very severe scalp psoriasis requiring systemic treatment, known allergy to any study intervention; immunosuppression; history of adverse response to topical or systemic steroid therapy

<table>
<tr><th>Mean baseline</th><th>Clobetasol propionate
N = 76</th><th>Calcipotriol N = 75</th></tr>
<tr><td>Age, years (mean±SD)</td><td>44.9±16.8</td><td>45.7±17.4</td></tr>
<tr><td>Gender M/F</td><td>49/51</td><td>45/55</td></tr>
<tr><td>TSS (mean ±</td><td>4.86±1.95</td><td>4.95±1.49</td></tr>
</table>
</td>
<td>Clobetasol propionate shampoo 0.05%

(N=76)

Formulation: shampoo

Frequency:

once daily (to a dry scalp – rinse off after 15 mins)</td>
<td>Calcipotriol solution 0.005%

(N=75)

Formulation: scalp solution

Frequency:

twice daily (to a dry scalp – without rinsing)

BOTH ARMS: concomitant use of</td>
<td>Treated for 4 weeks</td>
<td>Assessed at baseline, week 2 and week 4

1° outcomes:

Global and total severity scores (GSS and TSS)

GSS: 0 (none) to 5 (very severe)

2° and other outcomes</td>
<td>Galderma R&D</td>
</tr>
</table>

<table>
<tr>
<td>psoriasis. J.Dermatol. Treat. 16 (1):31-36, 2005.
Ref ID: REYGAGNE 2005</td>
<td>• Sample size calculation. Yes. 50 per group gives 90% power to detect a 1.5 point difference on TSS at a two-sided 5% significance level

• ITT analysis Yes for efficacy, but not AEs.</td>
<td>s:

9 in clobetasol group and 14 in calcipotriol group excluded from per protocol analysis</td>
<td>
<table>
<tr><td>SD)</td><td></td><td></td></tr>
<tr><td>GSS (mean ± SD)</td><td>3.49±0.60</td><td>3.51±0.60</td></tr>
<tr><td>% scalp area affected (mean ± SD)</td><td>46±28</td><td>44±28</td></tr>
</table>
</td>
<td></td>
<td>topical or systemic psoriasis treatments (except emollients, tars or salicylic acid for other sites) or drugs that could aggravate psoriasis (b-blockers, lithium, anti-malarials or NSAIDs) not permitted</td>
<td></td>
<td>:

IAGI (worse to cleared);

Adverse events</td>
<td></td>
</tr>
<tr>
<td colspan="8">Effect Size

Outcomes

<u>Efficacy</u> (ITT population: clobetasol propionate N = 76 calcipotriol N = 75)
<table>
<tr><th></th><th>Clobetasol propionate
N = 76</th><th>Calcipotriol
N = 75</th><th>p-value</th></tr>
</table>
</td>
</tr>
</table>

% clear or nearly clear at wk 4 on **IAGI**	38 (50%)	21 (28.4%)	0.003
% clear or nearly clear at wk 4 on **PAGI**	36 (47.3%)	23 (31.1%)	0.009

Time to effect

- Graphical representation of mean TSS over time shows that clobetasol propionate acts more quickly, with a large effect by week 2 which begins to slow between weeks 2-4. Calcipotriol has a more constant reduction in mean TSS, which has not reached a plateau by the end of the trial (4 weeks)

Withdrawals

	Clobetasol propionate **N = 76**	**Calcipotriol** **N = 75**
Withdrawal due to adverse events	0	7

Adverse events

Skin atrophy, n (%)	**Clobetasol propionate**	**Calcipotriol**

Baseline	**N = 76**	**N = 75**
Edge of scalp	3 (3.9%)	**0**
Face	5 (6.6%)	**0**
Neck	1 (1.3%)	**2 (2.7%)**
Week 4 *	**N = 74**	**N = 64**
Edge of scalp	1 (1.4%)	0
Face	4 (5.4%)	0
Neck	1 (1.4%)	1 (1.6%)

Authors conclusion

- Short contact therapy of scalp psoriasis with this new shampoo formulation of clobetasol propionate was significantly more effective and better tolerated than calcipotriol solution for the treatment of scalp 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>Klaber MR, Hutchinson PE, Pedvis-Leftick A, Kragballe K, Reunala TL, Van de Kerkhof PC, Johnsson MK, Molin L, Corbett MS, Downess N. Comparative effects of calcipotriol solution (50 micrograms/ml) and betamethasone 17-valerate solution (1 mg/ml) in the treatment of scalp psoriasis. Br J Dermatol.</td>
<td>Multicentre (Canada, Denmark, Finland, the Netherlands, Norway, Sweden, UK)

SCALP PSORIASIS

DESIGN
Between patient
Patient delivery
ALLOCATION
Random
Method of randomisation: (method unclear)
Concealment: unclear</td>
<td>N=474

Drop-outs (don’t complete the study):
N=29 (6.1%): 20 (8.3%) calcipotriol; 9 (3.8%) betamethasone

Reasons:
N=13 Adverse events (N=11 calcipotriol; N=2 betamethasone) N=6 unacceptable</td>
<td>INCLUSION CRITERIA
Adults; stable, mild-to-moderate scalp psoriasis; history of psoriasis on body

EXCLUSION CRITERIA
More extensive, severe or infected psoriasis; recent systemic antipsoriatic treatment or UV; concurrent vitamin D, calcium or other relevant medication; significant hepatic or renal disease; hypercalcaemia; risk of pregnancy; pregnancy; lactation
<table>
<tr><th></th><th>Calcipotriol (n=240)</th><th>Betamethasone (n=234)</th></tr>
<tr><td>Age (years)
Mean (SD)
Range</td><td>45.2 (15.9)
18 – 90</td><td>42.9 (15.5)
18 – 83</td></tr>
<tr><td>Sex
Males (%)</td><td>53.3
46.7</td><td>49.6
50.4</td></tr>
</table>
</td>
<td>N=240

Calcipotriol solution (50 µg/ml)

Formulation:
scalp solution

Frequency: Twice daily (maximum amount allowed was 60 ml)

Amount of medication used:
Patients used a mean (±SD) of 31.5 (±16.9) ml per week in the</td>
<td>N=234

Betamethasone 17-valerate solution (1 mg/ml)

Formulation
scalp solution

Frequency:
Twice daily (maximum amount allowed was 60 ml)</td>
<td>Double-blind treatment duration: 4 weeks (evaluated at 1, 2, 4 weeks).

After this time, patients who required no further treatment were observed for 4 weeks for relapse.</td>
<td>Assessment of extent of scalp psoriasis (graded 0-5)

Total sign score (erythema, thickness, scaliness [each graded 0-4 for overall score of 0 to 12])

Investigator global</td>
<td>Leo Pharmaceutical Products, Denmark</td>
</tr>
</table>

1994;131(5):678-83. REF ID: KLABER1994	BLINDING Double-blind (patient / assessor) WITHDRAWAL / DROPOUT Described • **Setting:** Not stated • **Washout period**: 2 weeks • **Sample size calculation** Yes. Study designed to detect an absolute difference of 10% with a power of 80% and a significance level of 5% between the two treatment arms with	treatment response (N=4 calcipotriol ; N=2 betamethasone) N=10 default (N=5 calcipotriol ; N=5 betamethasone)	<table><tr><td>Females (%)</td><td></td><td></td></tr><tr><td>Duration of scalp psoriasis (years) Mean (SD) Range</td><td>13.1 (11.0) 0.1 – 52.0</td><td>13.1 (11.3) 0.1 – 67.0</td></tr><tr><td>Score for extent Mean (SD) Range</td><td>2.7 (1.3) 1 – 5</td><td>2.8 (1.3) 1 – 5</td></tr><tr><td>Total sign score* Mean (SD) Range</td><td>6.4 (1.7) 3 – 12</td><td>6.6 (1.7) 2 – 12</td></tr></table> *Sum of scores for erythema, thickness and scaliness	calcipotriol group, and 27.1 (±17.5) ml per week in the betamethasone group (p=0.014).		Retreatment for further 6 weeks was offered to patients who relapsed and who were originally in the calcipotriol-treated group	assessment (5-pt: worse to cleared) Patient global assessment (5-pt: worse to cleared) Adverse events Compliance Relapse rate	

	respect to the proportion of patients who attain either clearance or marked improvement according to investigators overall assessment • **ITT analysis** Yes (adverse events); No (efficacy)							

Effect Size

Outcomes

<u>Efficacy</u>

	Calcipotriol (n = 236)	Betamethasone (n = 232)	95% CI of difference	P value
Investigator global assessment at week 4 'marked improvement or cleared'	138 (58.5%)	175 (75.4%)	25.3 – 8.6	<0.001

Patient global assessment at week 4 'marked improvement or cleared'	136 (57.6%)	171 (73.7%)	24.6 – 7.6	<0.001

Time to effect

Score for extent and total sign score decreased significantly from baseline at week one (and all subsequent time points) for both treatment groups (displayed graphically).

Time to max effect

TSS had not reached a minimum for either treatment group at week 4

Compliance

Compliance was good in both groups and >90% of patients were fully compliant at each follow-up visit. Patients used a mean of 31.5 (±16.9) ml per week in the calcipotriol group and 27.1 (±17.5) ml per week in the betamethasone group (p = 0.014)

Toxicity

Prematurely discontinued treatment

	Calcipotriol (n = 240)	Betamethasone (n = 234)
Adverse event s	11 (4.6%)	2 (0.85%)
Unacceptable treatment response	4 (1.7%)	2 (0.85%)
Default	5 (2.1%)	5 (2.1%)

Adverse events

	Calcipotriol (n = 240) No. of adverse events (%)	Betamethasone (n = 234) No. of adverse events (%)	P
Lesional or perilesional irritation	62 (25.8)	19 (8.1)	<0.001
Facial irritation	27 (11.3)	1 (0.4)	<0.001
Various skin reactions	6 (2.5)	9 (3.08)	NS
Non-cutaneous	3 (1.2)	6 (2.5)	NS
No. of patients reporting ≥1 adverse event	87 (36.3)	31 (13.2)	<0.001

There were no consistent or clinically important differences between the calcipotriol- and betamethasone-treated groups with regard to haemopoietic, liver or renal function. In particular there was no change in the mean serum total calcium in either group during the double-blind treatment.

Post treatment follow-up and re-treatment

	Calcipotriol (n = 99)	Betamethasone (n = 129)	95% CI of difference	P value
Relapse rate after 4 weeks observation (defined as an increase in the total sign score to at least 50% of the score at the start of double-blind treatment)	75 (75.8%)	102 (79.1%)		NS
Received retreatment with calcipotriol for 6 weeks	n = 69			
Patient global assessment at end of retreatment	82.6%			

'marked improvement or cleared'				
TSS Mean % reduction in score from relapse to end of retreatment	60.1%		51.8 – 68.4	<0.001

There was no change in serum calcium during retreatment

Summary

- Calcipotriol solution was effective in treating mild to moderate scalp psoriasis. However, betamethasone solution was significantly more effective, and was associated with statistically significantly less local irritation on the scalp and face

H.7.3 VITAMIN D OR VITAMIN D ANALOGUE VS TAR

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Klaber MR, McKinnon C. "Calcipotriol (DovonexR) scalp solution in the treatment of scalp psoriasis: Comparative efficacy with 1% coal tar/1% coconut oil/0.5% salicylic acid (CapasalR) shampoo,	Multicentre SCALP PSORIASIS • **Setting:** hospital out-patients and primary care patients • **Randomised** method unclear • **Washout period**: not stated	N: 475 **Drop-outs (don't complete the study):** N =141: 72 (30.3%) calcipotriol; 69 (29.1%) tar **Reasons:** N=32 Loss to follow-up (N=12 Calcipotri	**INCLUSION CRITERIA** **Mild or moderate** scalp psoriasis; ≥18 years old **EXCLUSION CRITERIA** Other forms of psoriasis; topical antipsoriatic treatment within previous 2 wks; systemic antipsoriatic treatment or UV therapy within previous 4 wks; concomitant vitamins, calcium or other medications that could affect the course of psoriasis; known hypersensitivity to study medications; pregnancy; inadequate contraception; lactation; hypercalcaemia; significant renal or hepatic disease **Mean baseline** / **Calcipotriol N = 238** / **Coal Tar N = 237** Age, years: 45.8±15.6 / 44.7±16.1	N=238 Calcipotriol solution, 50 µg/g, (Dovonex®) **Formulation**: scalp solution **Frequency:** twice daily (to a dry scalp after washing)	N=237 Coal tar,1%, coconut oil, 1%, salicylic acid, 0.5%, shampoo (Capasal®) **Formulation**: shampoo **Frequency:** once daily (leave for a few minutes before	Treatment duration: 8 weeks. + 16 weeks further treatment for those who received calcipotriol scalp solution and showed at least slight improvement	IAGI (6 pt: worse to cleared) Patients global assessment of disease severity (VAS) AEs	Leo Pharmaceuticals

and long-term experience." *Journal Of Dermatological Treatment* 2000;**11**(1): 21–8. REF ID:MCKINNON2000	• **Blinding** No. Open study • **Allocation concealment**. Unclear • **Sample size calculation**. Unclear • **ITT analysis** No	ol; N=20 Coal tar). N=20 stopping medication for >7 days (N=16 Calcipotriol; N=4 Coal Tar) Plus 35 and 16 for calcipotriol and coal tar respectively for adverse events (Note: may be classified under >1 reason)	(mean±SD)				washing out) **Note:** Alphosyl HC was applied twice daily to any psoriasis on the trunk and limbs in this group			
			Gender M/F%	52/48	52/48					
			TSS (mean ± SD) (0-12)	5.1±1.4	5.0±1.6					
			Caucasian	98.3%	98.3%					

Effect Size

Outcomes

Efficacy (available case analysis)

0-8 weeks	Calcipotriol (n=210)	Coal Tar (n=213)	OR (95% CI)	p-value
IAGI (at least moderate improvement) (6 pt: worse to cleared)	120 (57%)	79 (37%)	3.2 (2.0-5.2)	<0.001

- N = 166 Calcipotriol-treated patients, who had shown at least slight improvement entered the long-term treatment phase. For these patients, the mean change in TSS from baseline to 8 weeks was -2.2 and week 8 to 24 was -1.0. p<0.05 16 versus 8 weeks.

Time to effect

- During the 8 wk comparative phase graphical information shows that based on change in TSS both treatments had not reached maximum effect by the end of 8 weeks
- Over the long-term treatment phase graphical information shows that based on change in TSS calcipotriol reaches maximal effect by 12 weeks, with only slight further improvement up to 24 wks (<0.5 point reduction on TSS over 12 weeks)

Toxicity

	Calcipotriol (8wks) **N=230** (during comparative treatment)	Coal Tar **N=215** (during comparative treatment)	Calcipotriol (16wks) **N=166** (long-term treatment)
Withdrawal due to adverse events	35 (15.2%)	16 (7.4%)	6 (3.6%)

Summary

- Calcipotriol scalp solution is more effective than a coal tar-based shampoo and shows continued efficacy and good tolerability with long-term use.

H.7.4 VITAMIN D OR VITAMIN D ANALOGUE VS PLACEBO

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Green C, Ganpule M, Harris D, Kavanagh G, Kennedy C, Mallett R, et al. Comparative Effects of Calcipotriol (Mc903) Solution and Placebo (Vehicle of Mc903) in the Treatment of Psoriasis of the Scalp. *British Journal Of Dermatology* 1994;130(4):483–7.	**RCT** **DESIGN** Between patient Patient delivery **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (patient / investigator) • **Washout period:** 2 weeks • **Sample size calculation** not stated	**Total N:** 49 **Drop-outs (don't complete the study):** Total = 3 (6.1%) 1 active group had local side effects of erythema, itching and scalp flaking; 2 in placebo group withdrew due to inadequate response	INCLUSION CRITERIA Mild to moderate scalp psoriasis and a history of psoriasis elsewhere on the body; adult. EXCLUSION CRITERIA Excessively thick scalp psoriasis. Other scalp disease; marked deterioration of scalp psoriasis at entry; recent systemic or UV therapy; concurrent topical corticosteroid use; vitamin D or calcium supplement; medications which could affect the course of the disease; hypercalcaemia; hepatic or renal disease; at risk of pregnancy BC: unclear (not reported in full; only reported as "well matched at baseline for age, sex, history of psoriasis and extent and severity of scalp psoriasis)	**n=25** **Calcipotriol solution, 50mcg/ml, BD** **Formulation:** solution **Class:** vitamin D analogue **Frequency:** twice daily **Amount used:** not stated	**n=24** **Placebo (vehicle)** **Formulation**: solution **Frequency:** twice daily	**Treatment duration:** 4 weeks **Assessments at:** week -2, 0, 1, 2 and 4 **Follow-up after end of treatment:** none	Investigator global assessment (Extent of psoriasis: 0=none to 5=80-100%; treatment response: -1 worse, no change, slight improvement, marked improvement, cleared)) Patient global assessment and	Leo Pharmaceutical Products

Ref ID: GREEN1994	• **ITT analysis:** yes **Setting:** Outpatients		Age: not reported Gender (%M): not reported Severity: mean TSS (0 to 12): 6.7				scalp flaking/ itching (0-3 scale) **Primary efficacy parameter :** not stated	

Effect Size

Outcomes

<u>Efficacy</u>
Results presented graphically

	Calcipotriol N=25	**Placebo N=24**	**95% CI for difference**	**p value**
Investigator global assessment			19.0 to 67.6	<0.001
Patient global assessment			18.3 to 68.0	<0.001

IAGI (Clearance or marked improvement)	15 (60%)	4 (17%)		
PAGI (Clearance or marked improvement)	Only reported graphically			

Time-to-effect: Mean TSS still reducing at week 4

Withdrawals

Withdrawal due to inadequate response	2 in placebo group
Withdrawal due to AEs	1 active group had local side effects of erythema, itching and scalp flaking

Authors' conclusion

Calcipotriol was superior to Placebo in reducing redness, thickness, scaliness, extent of psoriasis, and scalp flaking and itching.

H.7.5 PIMECROLIMUS VS PLACEBO

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
C. Gribetz, M. Ling, M. Lebwohl, D. Pariser, Z. Draelos, A. B. Gottlieb,	RCT Multicentre (7 centres in USA)	Total N: **57** **Drop-outs (don't complete**	**INCLUSION CRITERIA** Stable, chronic plaque psoriasis; **moderate to severe** inverse psoriasis affecting axillae, inguinal, inframammary or gluteal cleft regions	(N=28) **Pimecrolimus** 1% (Elidel®)	(N=29) **Placebo/vehicle of identical appearance**	Treated for 8 weeks	IGA score : recorded at each visit using a 5 point	Novartis Pharmaceuticals Group

N. Zaias, D. M. Chen, A. Parneix-Spake, T. Hultsch, and A. Menter. Pimecrolimus cream 1% in the treatment of intertriginous psoriasis: a double-blind, randomized study. J.Am.Acad.Dermatol. 51 (5):731-738, 2004. Ref ID: GRIBETZ2004	INVERSE/FLEXURAL PSORIASIS DESIGN Between patient Patient delivery ALLOCATION Random Method of randomisation: 'validated system that automates the random assignment of treatment codes'. Concealment: Adequate (randomisation code kept confidential) BLINDING Double-blind (patient / investigator); adequately defined	**the study): 6** 2 (7.1%) on pimecrolimus and 4 (13.8%) on placebo **Reasons** See below	(duration ≥ 6 months); PGA ≥ 3; erythema ≥2; aged ≥ 18 **EXCLUSION CRITERIA** Clinically significant laboratory abnormalities; hypersensitivity to study drug or vehicle; systemic, phototherapy or immuno-modifying agents within previous 30 dys; topical therapies within previous 14 dys; unstable plaque psoriasis, pustular, drug associated or erythrodermic psoriasis BC: Yes Age: 47.8 (range: 21 to 88) Gender (%M): 50.9% Severity: PGA, % moderate: 72% PGA, % severe: 29.8% TSS: 5.34 (range: 3.0 to 9.0)	**Formulation**: cream **Frequency:** twice daily (~12h apart)	**Formulation**: cream **Frequency:** twice daily (~12h apart) ---------- **BOTH ARMS:** study medication applied to all study sites areas; no concomitant medications in intertriginious areas (except bland emollients)		scale: 0(clear)=no signs of inverse psoriasis except for residual discolouration; 1 (almost clear)=just perceptible erythema, no induration, and no scaling; 2 (mild disease)=mild erythema, no induration, and mild or no scaling; 3 (moderate disease)=moderate erythema, mild induration, and mild or no	

	• **Washout period**: 'appropriate' washout period of other medications (see exclusion criteria) • **Sample size calculation**. No • **ITT analysis** Yes – LOCF (including all randomised patients who took at least one dose of study medication and had at least one post-baseline efficacy assessment).				**Concomitant** use of existing topical therapies (low-to-mid potency corticosteroids, tazarotene and calcipotriene) allowed to non-study sites		scaling; and 4 (severe disease)= severe erythema, moderate to severe induartion, and mild or no scaling; and 4 (severe disease)= severe erythema, moderate to severe induartion and scaling of any degree. Adverse events (including skin atrophy) and withdrawal	

							S	

Effect Size

Outcomes

Efficacy (ITT population)

IGA (Investigators Global Assessment) & time to effect

Percentage of patients with IGA score 0 or 1 at each visit (0=clear, 1=almost clear)	**Pimecrolimus N=28**	**Vehicle N=29**	**p-value**
baseline	**0**	**0**	
Day 3	**14.3**	**0**	**p=0.04**
Day 7	**35.7**	**13.8**	**P=0.07**
Week 2	**53.6**	**20.7**	**P=0.01**
Week 4	**64.3**	**20.7**	**p=0.001**
Week 6	**67.9**	**17.2**	**P<0.0001**
Week 8	**71.4**	**20.7**	**P<0.0001**

Withdrawals

	Pimecrolimus (N=28)	**Placebo** **N=29**
Withdrawal due to adverse events	0	0
Withdrawal due to lack of efficacy	1	2
Withdrawal (other)	1	2

Adverse events

	Pimecrolimus (N=28)	**Placebo** **N=29**
Skin atrophy, n (%)	**0**	**0**

Authors conclusion

- Pimecrolimus cream 1% is an effective treatment for inverse psoriasis with a rapid onset of action, and is safe and well-tolerated.

H.7.6 TACROLIMUS VS PLACEBO

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Lebwohl M, Freeman AK, Chapman MS, Feldman SR, Hartle JE, Henning A; Tacrolimus Ointment Study Group. Tacrolimus ointment is effective for facial and intertriginous psoriasis. *J Am Acad Dermatol.* 2004;51(5): 723-30. REF ID:	Multicentre (USA) FACIAL AND INTERTRIGINOUS PSORIASIS DESIGN Between patient Patient delivery ALLOCATION Random Method of randomisation: not reported Concealment: unclear BLINDING	N=167 **Drop-outs (don't complete the study):** N=30 (18%): 14 (12.5%) tacrolimus; 16 (29.1%) vehicle **Reasons:** N=1 adverse event – non-treated area (N=1 vehicle). N=6 lack of	**INCLUSION CRITERIA** Age limit unclear (stated as ≥2 and ≥16); chronic plaque psoriasis affecting intertriginous and facial skin; disease stable or slowly worsening for ≥1 wk; target lesion of moderate erythema and TSS (0 to 12) ≥4 **EXCLUSION CRITERIA** Systemic therapy or phototherapy within previous four wks; topical therapy within previous two wks; inhaled / intranasal corticosteroids within previous two wks; other topical agents (excluding sunscreen)within previous one day; recently diagnosed (< six months) or recent exacerbation of inverse psoriasis; uncontrolled chronic co-morbidity; pregnancy; lactation; previous use of tacrolimus ointment for facial or intertriginous psoriasis	N=112 0.1% tacrolimus ointment **Formulation**: Ointment **Frequency:** Twice daily (thin layer of ointment to all areas of active disease on the face or intertriginous areas as defined by the investigator at baseline)	N=55 Vehicle **Formulation** Ointment **Frequency:** Twice daily (thin layer of ointment to all areas of active disease on the face or intertriginous areas as defined by the investigator at baseline)	Treatment duration: 8 weeks (evaluated: days 1, 8, 15, 29, 43, 57 or end of treatment)	Inverse psoriasis severity score (Static Severity Score; SSS) (6 pt: clear to very severe) IAGI ('PGA')(7 pt: exacerbation to clear) Adverse events	Fujisawa Healthcare, Inc

<table>
<tr>
<td>LEBWOHL2004</td>
<td>Double-blind (patient / investigator)

WITHDRAWAL / DROPOUT

Described

• Setting: Not stated

• Washout period: see exclusion criteria

• Sample size calculation. Not stated

• ITT analysis Yes. All patients received at least one dose of study drug and had ≥1 follow-up visit and were included in</td>
<td>efficacy (N=6 vehicle). N=11 Lost to follow-up (N=7 tacrolimus; N=4 vehicle). N=12 Other reasons(including patient decision, non-compliance and ineligibility) (N=7 tacrolimus; N=5 vehicle)</td>
<td>
<table>
<tr><td></td><td>Tacrolimus ointment (n = 112)</td><td>Vehicle (n = 55)</td></tr>
<tr><td>Gender
Male
Female</td><td>
70 (62.5%)
42 (37.5%)</td><td>
28 (50.9%)
27 (49.1%)</td></tr>
<tr><td>Race
White
African America
Other</td><td>
96 (85.7%)
8 (7.1%)
8 (7.1%)</td><td>
46 (83.6%)
6 (10.9%)
3 (5.5%)</td></tr>
<tr><td>Age (y)
Mean ± SD</td><td>48.0±15.7</td><td>48.0±15.6</td></tr>
<tr><td>Static severity score Median range</td><td>3 (1.5–5)</td><td>3 (1.5–4.5)</td></tr>
<tr><td>Concurrent plaque-type lesions</td><td>96 (85.7%)</td><td>46 (83.6%)</td></tr>
</table>
</td>
<td>Note:
Patients were instructed to continue topical treatment of their plaque-type psoriasis in other body-sites with their current treatment regimen

The use of lithium, tricyclic antidepressants, beta-blockers and oral antihistimines was permitted during study if patient was receiving stable dose at baseline.</td>
<td></td>
<td></td>
<td>Withdrawals</td>
<td></td>
</tr>
</table>

	analysis							

Effect Size

Outcomes

Efficacy

	Tacrolimus ointment (n = 112)	Vehicle (n = 55)	P value
PGA Clinical improvement ≥90% (excellent improvement or clearing) at day 57	66.7%	36.8%	= 0.002
SSS Clear or almost clear at day 57	73 (65.2%)	17 (31.5%)	<0.0001
Total disease signs and symptoms score of 0 at day 57	45.5%	11.1%	<0.0001

Disease signs and symptoms score for the target lesions at the end of the study

	Tacrolimus ointment (n = 112)	Vehicle (n = 54)	P value
Erythema	0.5	1.8	<0.0001
Induration	0	1.0	<0.0001
Desquamation	0	1.0	<0.0003
Overall severity	0.5	1.5	<0.0001

Time to effect

Tacrolimus ointment was associated with significant improvements on the PGA and SSS at day 8 (first evaluation after baseline) in 24.8% compared with 6% in vehicle group.

	Tacrolimus ointment (n = 112)	Vehicle (n = 55)	P value
PGA Clinical improvement ≥90% (excellent improvement or clearing) at day 8	24.8%	6%	= 0.004
SSS	Not stated	Not stated	= 0.001

Time to max effect

Percentage of patients with rating of 'excellent improvement' or 'clearing' for PGA was highest for both vehicle and tacrolimus ointment at day 57

(displayed graphically); although there was only modest improvement (<5% increase in numbers achieving success) from day 29.

Toxicity

Prematurely discontinued treatment

	Tacrolimus ointment (n = 112)	Vehicle (n = 55)
Adverse event – treated area	0	0
Adverse event – non-treated area	0	1 (1.8%)
Lack of efficacy	0	6 (10.9%)
Lost to follow-up	7 (6.3%)	4 (7.3%)
Other*	7 (6.3%)	5 (9.1%)

*Other reasons include patient decision, non-compliance and ineligibility

Incidence rate of reported or observed drug-related adverse events occurring in >2% of the study population

	Tacrolimus ointment (n = 112)	Vehicle (n = 55)	P value
Burning or stinging	9 (8.0%)	4 (7.3%)	1.00
Hyperesthesia	5 (4.5%)	0	0.17
Itching	8 (7.1%)	1 (1.8%)	0.27

These three adverse events occurred on average within the first three days of treatment for both treatment groups, excluding burning/stinging in the tacrolimus ointment-treated group, which had a mean time to onset of 10 days.
There were no reports of cutaneous infections or systemic adverse events

Authors conclusion

- Tacrolimus ointment (0.1%) is an effective treatment for psoriasis of the face or intertriginous areas

H.7.7 TACROLIMUS VS VITAMIN D OR VITAMIN D ANALOGUE

<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>Y. H. Liao, H. C. Chiu, Y. S. Tseng, and T. F. Tsai. Compariso n of cutaneous tolerance and efficacy of calcitriol 3 microg g(-1) ointment and tacrolimus 0.3 mg g(-1) ointment in chronic plaque psoriasis involving facial or genitofemo ral areas: a double-blind,</td>
<td>RCT

Single centre

Parallel group

FACIAL or GENITOFEMOR AL PSORIASIS

• Setting: out-patient

• Randomised

Computer-generated (ratio 1:1).

• Washout period: 1 wk for topicals; 2 wk for UV; 4 wk for</td>
<td>Total N: 50

Drop-outs (don’t complete the study):

Calcitriol: 3 (12%)

Tacrolimu s: 0%

Reasons: non-medical</td>
<td>Inclusion criteria: aged ≥ 18 years; diagnosis of chronic plaque psoriasis affecting the face and/or gentiofemoral area.

Exclusion criteria: Underlying conditions requiring systemic calcium or vitamin D supplements; use of systemic treatments known to worsen psoriasis

<table>
<tr><th>Mean baseline</th><th>Calcitriol
N = 24</th><th>Tacrolimus
N = 25</th></tr>
<tr><td>Age, years (mean±SD)</td><td>41.6±14.0</td><td>37.7±11.5</td></tr>
<tr><td>Gender M/F%</td><td>79.2/20.8</td><td>68/32</td></tr>
<tr><td colspan="3">Target lesion</td></tr>
</table>
</td>
<td>Calcitriol 3 µg/g (Silkis)

(N=25)

Formulation: ointment

Frequency:

twice daily</td>
<td>Tacrolimus 0.3 mg/g (Protopic)

(N=25)

Formulation: ointment

Frequency:

twice daily

BOTH ARMS: no concomitant topical agents (including emollients)</td>
<td>Treated for up to 6 weeks</td>
<td>IAGI: 7-pt scale

Clear (100% improvem ent); nearly clear (90%); marked improvem ent (75%); moderate improvem ent (~50%); minimal improvem ent (~25%); no change; worse</td>
<td>Galder ma</td>
</tr>
</table>

randomized controlled trial. Br.J.Dermatol. 157 (5):1005-1012, 2007. Ref ID: LIAO2007	systemics • **Double blind** – adequately described • **Allocation concealment**. Unclear • **Sample size calculation**.Not stated • **ITT analysis** Yes (LOCF).		Face Gentiofemoral 22 (91.7%) 2 (8.3%) 22 (88%) 3 (12%) TSS 0-12 (mean±SD) 6.88±1.88 5.76±2.68		Only lesions in facial or gentiofemoral areas were treated using the investigational product Standard topical regimens on other body areas were permitted Irritancy sufficient to interfere with usual activity resulted in reduction in dose frequency to once daily (severe irritancy lead to discontinuation of study medication)		Withdrawals	

Effect Size

Outcomes

Efficacy

IAGI ITT population (LOCF)	Calcitriol N = 24	Tacrolimus N = 25	p-value for difference
Clear or nearly clear	8 (33.3%)	15 (60%)	<0.05

Time to effect

- Graphical representation of % change in TSS over time shows that both treatments reached maximum effect by week 4, with negligible further improvement between wk 4 and 6)

Author's conclusion

- Both calcitriol and tacrolimus are safe and well tolerated in the treatment of psoriasis in sensitive areas
- Tacrolimus demonstrated better clinical efficacy

H.7.8 TAR VS CORTICOSTEROID

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
C. E. Griffiths, A.	RCT	Total N: **162**	**Inclusion criteria:** aged ≥ 18 years; **moderate-to-severe** scalp psoriasis	Clobetasol propionate	Tar blend shampoo	Treated for 4	**1° outcome:**	Not stated

<table>
<tr>
<td>Y. Finlay, C. J. Fleming, J. N. Barker, F. Mizzi, and S. Arsonnaud. A randomized, investigator-masked clinical evaluation of the efficacy and safety of clobetasol propionate 0.05% shampoo and tar blend 1% shampoo in the treatment of moderate to severe scalp psoriasis. J.Dermatol. Treat. 17 (2):90-95, 2006.</td>
<td>Multicentre

Parallel group

SCALP PSORIASIS

• Setting: unclear

• Randomised

Method not stated (ratio 3:1).

• Washout period: ‘subjects were asked to avoid excessive UV exposure and yo respect specified wash-out periods for systemic therapies for psoriasis’

• Single blind –</td>
<td>Drop-outs (don’t complete the study): unclear</td>
<td>(affecting at least 15% of scalp area).

Exclusion criteria: immunosuppression; pregnancy; lactation; history of allergic reactions or contraindications to studied medications

<table>
<tr><th>Mean baseline</th><th>Clobetasol propionate
N = 121</th><th>Tar blend shampoo
N = 41</th></tr>
<tr><td>Age, years (mean±SD)</td><td>46.7±14.9</td><td>45.4±13.2</td></tr>
<tr><td>Gender M/F</td><td>48.8/51.2</td><td>65.9/34.1</td></tr>
<tr><td>Race – white, n (%)</td><td>116 (95.8%)</td><td>38 (92.7%)</td></tr>
<tr><td>TSS 0-9 (mean)</td><td>6.1</td><td>6.3</td></tr>
</table>
</td>
<td>shampoo 0.05%

(N=121)

Formulation: shampoo

Frequency:

once daily (to a dry scalp – rinse off after 15 mins)</td>
<td>(Polytar Liquid®: arachis oil extract of coal tar 0.3%, cade oil 0.3%, coal tar solution 0.1%, oleyl alcohol 1%, tar 0.3%)

(N=41)

Formulation: shampoo

Frequency:

twice weekly (to a wet scalp – followed by rinsing)

BOTH ARMS:</td>
<td>weeks</td>
<td>TSS: sum of scores for erythema, desquamated and thickness (each on a 0-3 scale); range: 0-9

2° and other outcomes:

Skin atrophy</td>
<td></td>
</tr>
</table>

Ref ID: GRIFFITHS2006A	investigator (no details) • **Allocation concealment**. Unclear • **Sample size calculation**. Yes. 90% power to detect a 1.5 point difference on TSS at a two-sided 5% significance level • **ITT analysis** Yes.				concomitant use of systemic psoriasis treatments or drugs that could aggravate psoriasis not permitted			

Effect Size

Outcomes

Efficacy

TSS (0-9) **ACA population**	**Clobetasol propionate**	**Tar blend shampoo**	**ANCOVA 95% CI**

(evaluable patients)	**N = 121**	**N = 41**	
Mean TSS at wk 4	3.1±1.9	5.3±1.9	-2.73, -1.41
TSS reduction at wk 4	50%	14.5%	

Sign score (0-3) **ITT population (LOCF)** **Mean±SD**	**Clobetasol propionate** **N = 121**	**Tar blend shampoo** **N = 41**	**p-value between groups**
Erythema			
Baseline	1.9±0.6	1.9±0.6	0.0001
Week 4	1.2±0.8	1.7±0.7	
Thickening			
Baseline	2.0±0.7	2.1±0.6	0.0001
Week 4	0.9±0.8	1.6±0.9	
Desquamation			
Baseline	2.2±0.6	2.3±0.5	0.0001
Week 4	1.1±0.8	1.9±0.8	

Time to maximum effect

- A small amount of continued improvement was seen between weeks 2 and 4 based on improvement in subjects' global assessment of improvement

from baseline for both treatments (with greater continued improvement for the clobetasol propionate group)

Withdrawals

	Clobetasol propionate **N = 121**	**Tar blend shampoo** **N = 41**
Withdrawal due to adverse events	1	0

Adverse events

	Clobetasol propionate **N = 121**	**Tar blend shampoo** **N = 41**
Skin atrophy, n	**0**	**0**

Author's conclusion

- Clobetasol propionate shampoo is superior to tar blend shampoo in the treatment of moderate-to-severe scalp psoriasis in terms of both efficacy and cosmetic acceptability

H.7.9 POTENT CORTICOSTEROID VS PLACEBO

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparisons	Length of follow-up	Outcome measures	Source of funding
Franz TJ, Parsell DA, Halualani RM, Hannigan JF, Kalbach JP, Harkonen WS. Betamethasone valerate foam 0.12%: a novel vehicle with enhanced delivery and efficacy. *Int J Dermatol.* 1999;38(8): 628-32. REF ID: FRANZ1999	Multicentre (USA) SCALP PSORIASIS DESIGN Between patient Patient delivery ALLOCATION Random Method of randomisation: unclear Concealment: unclear BLINDING Double-blind	N=190 **Drop-outs (don't complete the study):** N=18 **Reasons:** no details	**INCLUSION CRITERIA** Moderate to severe scalp psoriasis (each of 3 primary signs ((erythema, scaling, plaque thickness) ≥ 2); scalp involvement ≥10%; adults **EXCLUSION CRITERIA** Systemic psoriatic therapy within previous four wks; topical scalp preparations within previous two wks	N= 57 Betamethasone valerate (BMV) foam (0.1%) **Formulation**: foam **Frequency:** Twice daily to the entire scalp for 28 consecutive days **Note:** Patients were instructed to	N=58 BMV lotion (0.1%) **Formulation:** lotion **Frequency:** Twice daily --- N=28 Placebo foam **Formulation:** foam	28 days (evaluated at 2 and 4 weeks)	Erythema, scaling, thickness, pruritus IAGI (7 pt: worse to completely clear) PAGI (7 pt: worse to completely clear)	Conneticcs Corporation

	(patient / investigator) WITHDRAWAL / DROPOUT Described • **Setting:** No details • **Washout period**: see exclusion criteria • **Sample size calculation**: Not stated • **ITT analysis** Not stated			apply the study medication to the entire scalp; all patients were required to use DHS shampoo during the treatment phase. No other therapy to the scalp was allowed	**Frequency:** Twice daily N=29 Placebo lotion **Formulation:** lotion **Frequency:** Twice daily			

Baseline demographics

	BMV foam (n = 57)	BMV lotion (n = 58)	Placebo foam (n = 28)	Placebo lotion (n = 29)
Age				
Mean	46.6	48.6	50.8	48.5

18-59 (%)	70	78	68	69
>60(%)	30	22	32	31
Gender (%)				
Male	44	55	50	48
Female	56	45	50	52
Race (%)				
Caucasian	95	93	100	100
Hispanic	4	3	0	0
Other	1	4	0	0
Mean severity of disease (score 0-4)				
Scaling	2.75	2.67	2.93	2.83
Erythema	2.49	2.48	2.79	2.59
Plaque thickness	2.63	2.55	2.61	2.66

Effect Size

Outcomes

Efficacy

For each sign of psoriasis (scaling, plaque thickness, erythema), patients in the BMV foam group demonstrated significantly greater improvement after 28 days of treatment than did patients in the BMV lotion, placebo lotion or placebo foam groups (displayed graphically). The same trend was seen in the pruritus score, though the difference between BMV foam and BMV lotion was not statistically significant (displayed graphically)

% of patients completely clear or almost clear of disease at the end of treatment	BMV foam (n = 57)	BMV lotion (n = 58)	Placebo foam (n = 28)	Placebo lotion (n = 29)
IAGI	41 (72%*†)	27 (47%§)	6 (21%)	6 (21%)
PAGI	44 (77%*†)	27 (47%§)	6 (21%)	4 (14%)

*BMV foam vs placebo foam: p<0.05
†BMV foam vs BMV lotion: p<0.05
§BMV lotion vs placebo lotion: p<0.05

Time to max effect

Maximum effect was not reached for scaling, plaque thickness, pruritus and erythema scores by 28 days for all treatment groups (displayed graphically), with exception of placebo foam which was reached after 15 days for the scaling score.

Toxicity

No patients discontinued treatment during the study due to local skin reactions
Drug related complaints were burning, stinging, or itching at the site of application. Majority of these reactions were classified as mild. By the end of the treatment period, reports of local reactions at the site of application had diminished in both active treatment groups relative to the placebo groups. No patient discontinued treatment during the study due to local skin reactions.

Summary

- BMV foam was associated with significantly greater improvement after 28 days of treatment for scaling, erythema and plaque thickness scores of psoriasis compared to BMV lotion, placebo lotion or placebo foam

H.7.10 VERY POTENT CORTICOSTEROID VS PLACEBO

<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>Olsen AE, Cram DL, Ellis CN, Hickman JG, Jacobsen C, Jenkins EE, Lasser AE, et al. A double-blind, vehicle-controlled study of clobetasol propionate 0.05% (Temovate) scalp application in the treatment of moderate to severe scalp</td>
<td>DESIGN
Between patient
Patient delivery
SCALP
ALLOCATION
Random
Method of randomisation: not reported
Concealment: unclear
BLINDING
Double-blind (patient /</td>
<td>N: 378
Drop-outs (don’t complete the study): 1 did not complete one week of therapy (no reasons given and no group allocation reported).
27 did not attend the 1 week post treatment visit (5 in Clobetasol and 22 in placebo). Of the 5 Clobetasol patients not attending the post treatment session, 2 dropped out because of treatment failure, 2 due to unrelated medical problems and one because of non-compliance. Of</td>
<td>INCLUSION CRITERIA
Moderate to severe scalp psoriasis (TSS (0 to 9) ≥ 6); stable or worsening; adult.
EXCLUSION CRITERIA
Recent systemic, topical or UV treatment for psoriasis.
Baseline characteristics [mean(range) or proportion unless stated]:
<table>
<tr><th></th><th>Clobetasol</th><th>Placebo</th></tr>
<tr><td>Age</td><td>47 (19-88)</td><td>46 (18-88)</td></tr>
<tr><td>male</td><td>79/188</td><td>89/189</td></tr>
<tr><td>duration of psoriasis (yrs)</td><td>12.3 (0.4-50)</td><td>11.7 (1-55)</td></tr>
<tr><td>Severe disease</td><td>41/188</td><td>33/189</td></tr>
</table>
</td>
<td>Clobetasol propionate 0.05% BD, scalp application. A maximum of 50ml of study drug could be applied per week.
n= 188
Formulation:
solution
Frequency: Twice daily</td>
<td>Placebo (vehicle)
n= 189
Formulation: unclear
Frequency: Twice daily</td>
<td>Treatment duration: 2 weeks
Follow up: 3 weeks.</td>
<td>Outcomes assessed at 3,7, 14 days. Primary outcome time point should be 14 days, as only this point measured the effects of a whole course of therapy.
Investigator global assessment (6 pt: worse to cleared)</td>
<td>Glaxo Inc. Scalp trial</td>
</tr>
</table>

psoriasis. Journal of the American Academy of Dermatology 1991; 24:443-7 Ref ID: OLSEN1991	investigator) **WITHDRAWAL / DROPOUT** Described **Sample size calculation:** Not reported **ITT analysis:** Not reported	the 22 not attending the post treatment session, 17 dropped out because of treatment failure, 1 due to local irritation from the vehicle, 3 because of non-compliance and 1 was lost to follow-up. **Noncompliance:** 1 in the clobetasol group and 3 in the placebo group.	**Previous therapy**: Must have ceased systemic treatments for at least 4 weeks, and topical therapy for at least 2 weeks, prior to study entry.	**Concomitant therapies –** none reported			Patient global assessment (4 pt: poor to excellent) Adverse events Withdrawal due to adverse vents Withdrawal due to lack of efficacy	
Effect Size Outcomes **<u>Efficacy</u>**								

IAGI

	Clobetasol	**Placebo**
End of treatment – cleared or excellent	129/188	16/189
1 week post-treatment – cleared or excellent	114/183	13/167
End of treatment – good to excellent	152/188	42/189
1 week post-treatment – good to excellent	142/183	32/167

Adverse events

	Clobetasol	**Placebo**
Adverse events		
burning or stinging	21/188	18/189
scalp/ear papules	3/188	0/188
Increased pruritis	1/188	4/189
scalp tingling, tightness and hair loss	1/188	1/189
eye irritation	1/188	0/189
tightness	0/188	1/189
soreness	0/188	1/189
worsening of psoriasis	0/188	1/189

dryness	0/188	1/189

Withdrawals

	Clobetasol	**Placebo**
Withdrawal related to adverse events	0/188	1/189
Withdrawals due to lack of efficacy	2/188	17/189

Authors' conclusion: Clobetasol propionate 0.05% scalp application appears to be a safe and an effective treatment for scalp psoriasis.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Franz TJ, Parsell DA, Myers JA, Hannigan JF. Clobetasol propionate foam 0.05%: a novel vehicle with enhanced delivery. International Journal of dermatology 2000; 39: 521-538. **Ref ID: FRANZ2000**	**DESIGN** Between patient Patient delivery Multicentre **SCALP PSORIASIS** **ALLOCATION** Random Method of randomisation: not reported Concealment: unclear **BLINDING** Double-blind (patient / investigator)	Total N: 188 **Drop-outs (don't complete the study):** Total = 0 (0%) **Noncompliance:** Not reported	**PATIENT CHARACTERISTICS** N: 188 Baseline comparability: unclear; stated that groups well matched for age, gender and baseline severity. Age: not reported; all adult Gender (%M): 49.5% Severity: Mean TSS (0 to 12): 7.25 **INCLUSION CRITERIA** Moderate to severe scalp psoriasis (each of 3 primary signs [erythema, scaling, plaque thickness] ≥ 2); scalp involvement ≥10%; adults **EXCLUSION CRITERIA** Not reported	**Clobetasol propionate foam, 0.05% BD, or** **Clobetasol propionate lotion, 0.05% BD.** **Both manually applied to the whole scalp.** **n= 125** **Formulation**: Foam or solution **Frequency** twice daily	**Placebo** **n= 63** **Formulation** Foam or lotion **Frequency** twice daily	**Treatment duration:** 2 weeks **Follow up:** 4 weeks (from start of treatment)	Taken at 7, 14 and 28 days from start of treatment. Primary outcome point is 14 days, as that is when main outcomes data are presented. IAGI PAGI Adverse events withdrawal due to toxicity	Connectics Corporation

	Sample size calculation: Not reported **ITT analysis:** Not applicable		**Previous therapy**: Not reported	Concomitant therapies – They were required to use DHS shampoo. No other scalp therapy allowed.			Withdrawal due to lack of efficacy	

Effect Size

Outcomes

Efficacy

IAGI and PAGI at 14 days: Number completely clear or almost clear

	CP –foam or solution (n=125)	**Placebo – foam or solution (n=63)**	CP foam (n=62)	CP solution (n=63)	placebo foam (n=31)	placebo solution (n=32)
IAGI	**86/125**	**5/63**	46/62	40/63	3/31	2/32
PAGI	**77/125**	**4/63**	41/62	36/63	2/31	2/32

Time to max effect

Maximum effect was not reached for scaling, plaque thickness, pruritus and erythema scores by 14 days for all treatment groups (displayed graphically);

the mean severity score increased during the 14 days following removal of treatment

Adverse events

No difference between groups reported; no actual data given.

Withdrawal due to toxicity

None in either group

Withdrawal due to lack of efficacy

None in either group

Authors' conclusion

No conclusion was stated relating to CP versus placebo; however the improved efficacy of foam compared to solution was stated.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Poulin Y et al. Clobetasol propionate shampoo 0.05% is efficacious and safe for long-term control of moderate scalp psoriasis. J Dermatol Treat 2010; 21: 185-192. **Ref ID: POULIN2010**	**RCT** **DESIGN** Between patient Patient delivery **ALLOCATION** Random Method of randomisation: not stated Concealment: unclear **BLINDING** Open-label initial treatment phase (up to 4 weeks); then if GSS ≤2 (clear, very mild or mild) randomised to double-blind maintenance phase	**Total N: 168 entered treatment phase; 141 eligible for maintenance phase; 136 randomised** **Drop-outs (don't complete the study):** Total = (%): 9 (13.4%) active group and 17 (24.6%)	INCLUSION CRITERIA Moderate scalp psoriasis (global severity score 3 on a 0-5 scale) EXCLUSION CRITERIA Pregnant, nursing or planning a pregnancy Baseline comparability: yes Mean age 50 years 50% male 91.2% Caucasian; 6.6% Asian; 1.5% Hispanic; 0.7% other Global severity score: 15.4% clear; 47.8% very mild; 36.8% mild Erythema: 85.3% none-mild; 14.7% moderate-severe	**n=67** **Clobetasol propionate shampoo 0.05%** **Formulation:** short-contact shampoo formulation **Class:** super potent corticosteroid **Frequency:** once daily for initial treatment phase (4 weeks) and relapses (for 4 weeks); twice-weekly (3 days apart) in long-term remission/ maintenance	**n=69** **Vehicle** **Formulation**: short-contact shampoo formulation **Frequency:** twice-weekly in long-term remission/ maintenance	**Treatment duration:** initial treatment phase (up to 4 weeks); then if GSS ≤2 (clear, very mild or mild) randomised to double-blind maintenance phase up to 6 months **Assessments at:** every 4 weeks in maintenance phase	Relapse: GSS >2 (moderate, severe or very severe scalp psoriasis); investigator extent of disease (6-point scale) and individual sign scores (scaliness, erythema, plaque thickness) on a 5-point scale; patient assessment of pruritus intensity on 4-point scale; safety assessment (burning sensation, skin atrophy, telangiectasia, adverse	Galderma

	• **Washout period:** not applicable • **Sample size calculation :** not reported • **ITT analysis:** yes **Setting:** Outpatients	vehicle group (5 [7.5%] and 16 [23.2%] due to "patient's request"; 2 [3.0%] and 0 due to AE; 1 [1.5%] and 0 lost to follow up; 1 [1.5%] and 1 [1.4%] "other")	Scaliness: 88.9% none-mild; 11.1% moderate Plaque thickness: 97.1% none-mild; 2.9% moderate Extent of disease: 85.3% none to <20%; 14.7% 20-100% Pruritus: 96.4% none-mild; 3.6% moderate-severe	**Amount used:** applied to scalp as a thin film; left in place for 15 minutes before lathering and rinsing. During whole study (treatment + maintenance phase), clobetasol propionate shampoo 0.05% applied for 79.3 days in the CP group and 59.5 days in the vehicle group Note: during maintenance phase evaluation for relapse was every 4 weeks, if after 4 more weeks of once daily treatment disease control was not regained patients left the study, if control was regained the twice weekly maintenance		**Follow-up after end of treatment:** none	events), morning serum cortisol, patient satisfaction questionnaire ; time to first relapse; 5 of patients who had no relapse at each visit; total relapses in maintenance phase **Primary efficacy parameter:** not stated	

				schedule was re-instituted (further relapses were treated in the same manner)				

Effect Size

Outcomes

<u>Efficacy during maintenance phase</u> (for those achieving clear, very mild or mild during induction)

% patients with no relapse (GSS response maintained: mild, very mild or clear)

ITT (worst case population; those who discontinued before relapse were considered as having relapse at the next visit)	**Clobetasol propionate shampoo 0.05%** **n=67**	**Vehicle** **n=69**	**p value**
Baseline	100%	100%	-
1 month	71.6%	44.1%	p<0.01
2 months	61.2%	29.0%	p<0.01
3 months	58.2%	19.1%	p<0.01
4 months	50.0%	15.9%	p<0.01
5 months	44.8%	14.5%	p<0.01

6 months	40.3%	11.6%	p<0.01

Number of relapses by 6 months

	Clobetasol propionate shampoo 0.05% **n=67**	**Vehicle** **n=69**	**p value**
% patients who relapsed with only 1 relapse	73.2%	34.1%	p<0.001
2 relapses	16.8%	38.3%	
3 relapses	10.0%	27.6%	

	Clobetasol propionate shampoo 0.05% **n=67**	**Vehicle** **n=69**	**p value**
% patients with <20% of scalp affected at time of relapse	54.3%	38.6%	not stated
No pruritus at relapse	17.1%	3.5%	not stated
Median time to relapse	**141 days**	**30.5 days**	**<0.0001**

Patient satisfaction questionnaire

	Clobetasol propionate shampoo 0.05% **n=67**	**Vehicle** **n=69**	**p value**

Regime easy to incorporate into daily routine	100%	83.1%	not stated
Preferred twice-weekly treatment for a long period to daily treatment	72.7%	47.4%	p=0.004
Willing to continue treatment in the same way	86.0%		
Could adopt regimen for as long as a year	57.1%		
Treatment enough to control disease	73.7%	39.7%	p<0.001
Not bothered by side effects	93%	79.7%	p<0.05
Satisfied or very satisfied with overall treatment	84.2%	59.7%	p=0.006

Compliance: >95% both groups

Time-to-effect: 89% (141/168) of those entered into the induction phase achieved clear, mild or very mild disease after 4 weeks of treatment

Adverse events:

	Clobetasol propionate shampoo 0.05% **n=67**	**Vehicle** **n=69**	p value
Burning: 0 none 1 mild	 58 (86.6%) 7 (10.4%)	 56 (81.2%) 9 (13.0%)	0.063

2 moderate	2 (3.0%)	4 (5.8%)	
Skin atrophy 0 none 1 mild	 66 (98.5%) 1 (1.5%)	 69 (100%) -	0.527
Telangiectasia 0 none 1 mild (transient or already present at baseline)	 65 (97.0%) 2 (3.0%)	 68 (98.6%) 1 (1.4%)	0.806
Total AE (total 84 events in 57 people)	34 events (no. of people not stated)	50 events (no. of people not stated)	
Treatment-related AE	3 (1 asthma – severe treatment-related AE)	5	

No notable hypothalamic-pituitary-adrenal (HPA) axis suppression

Withdrawals

	Clobetasol propionate shampoo 0.05% **n=67**	**Vehicle** **n=69**
Withdrawal due to AEs	2 (3.0%)	0
Withdrawal due to “patient’s request”	5 (7.5%)	16 (23.2%)
Withdrawal due to loss to follow up	1 (1.5%)	0

Withdrawal other	1 (1.5%)	1 (1.4%)

Authors' conclusion

The regimen of Clobetasol propionate shampoo 0.05% once daily for initial treatment phase (4 weeks) and relapses (for 4 weeks) and twice-weekly (3 days apart) in long-term remission/ maintenance is efficacious and safe for long-term control of moderate scalp psoriasis.

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
Jarratt M, Breneman D, Gottlieb AB, Poulin Y, Liu Y, Foley V. Clobetasol propionate shampoo 0.05%: a new option to treat patients with moderate to severe scalp psoriasis. *J Drugs Dermatol.* 2004;3(4):367-73 REF ID: JARRATT2004	Multicentre (USA and Canada) SCALP PSORIASIS DESIGN Between patient Patient delivery ALLOCATION Random Method of randomisation: Computer generated list Concealment: unclear BLINDING	N=142 **Drop-outs (don't complete the study):** N=1 (not stated which arm they were allocated to) **Reason:** Applied a group III potent corticosteroid during washout period	**INCLUSION CRITERIA** Aged 12 or over; moderate to severe scalp psoriasis (global severity score ≥ 3); compliance with washout periods for systemic therapies (details not reported) **EXCLUSION CRITERIA** Pregnancy or risk thereof; known allergy to test products; need for systemic therapy or other concomitant antipsoriatics; excessive UV exposure	N=95 Clobetasol propionate shampoo, 0.05% **Formulation**: shampoo **Frequency:** Once daily **Note:** Treatments applied once a day and left on the dry scalp for 15 minutes, before lathering and rinsing	N=47 vehicle shampoo **Formulation** shampoo **Frequency:** Once daily	treatment duration: 4 weeks, followed by treatment free 2 week follow-up (patients told to avoid study medication and all psoriasis medications previously excluded)	The primary endpoint was the success rate after 4 weeks of treatment, defined as the proportion of subjects with a GSS of 0 or 1. Failure was defined as GSS of ≥2 Global severity score (GSS) (6 pt: clear	Galderma R&D Inc

	Double-blind (patient / investigator) WITHDRAWAL / DROPOUT Unclear • **Setting:** Not stated • **Washout period**: 2 weeks for systemic anti-psoriatic medications • **Sample size calculation**. Yes. 132 subjects were planned to be enrolled to collect sufficient safety data and to detect a significant difference in success rates			The use of topical emollients, coal tars, vitamin D derivatives, tazarotene or salicylic acid to treat body psoriasis during the course of the study was allowed			to very severe) IAGI (5 pt: worse to clear) PAGI (5 pt: worse to clear)	

	of 60% vs 20% with 90% power at the 0.05 significance level for the 2-tailed alternative, adjusting for a 10% dropout rate. • **ITT analysis** For efficacy endpoints							

Demographics

	Clobetasol propionate shampoo (n =95)	Clobetasol propionate shampoo vehicle (n=47)
Male/female (n)	38/57	22/25
Caucasian (n)	88	43
Black (n)	2	1
Hispanic (n)	4	3
Other (n)	1	0

Mean age ± SD (years)	45.1±15.3	45.1±15.7
Global severity score (full scaled		
Moderate	70	32
Severe	20	10
Very severe	5	5
Total severity score ± SD	6.5±1.1	6.7±1.2

Effect Size

Outcomes

Efficacy

	Clobetasol propionate shampoo (n = 95)	**Vehicle shampoo (n = 47)**	**P value**
Proportion of patients achieving 'success' (GSS clear or minimal) at 4 weeks	40 (42.1%)	1 (2.1%)	<0.001
Proportion of patients achieving 'success'(GSS clear or minimal) at 6 weeks	Significantly more patients in clobetasol propionate shampoo arm achieved 'success' compared to vehicle arm (no further details)		=0.003

- About 50% of subjects in the clobetasol propionate shampoo arm who achieved success at week 4 remained a treatment 'success' at the 2 week

follow-up

- There was no observation of rebound, defined as having achieved 'success' during treatment and then deteriorated to worse than pre-treatment levels.

	Clobetasol propionate shampoo (n = 95)	**Vehicle shampoo (n = 47)**	**P value**
GSS at 4 weeks – Proportion mild or better	68 (71.6%)	7 (14.9%)	<0.001
GSS at 4 weeks – Proportion clear	10 (10.5%)	0	<0.001
Investigator assessment at 4 weeks	Significantly better with clobetasol propionate shampoo compared to vehicle (depicted graphically)		<0.001
Subject assessment at 4 weeks	Significantly better with clobetasol propionate shampoo compared to vehicle (depicted graphically		<0.001

Time to effect

Score for TSS decreased significantly from baseline at week two (first evaluation after baseline) for clobetasol propionate shampoo subjects compared to vehicle control (displayed graphically).

Time to max effect

Score for TSS was most reduced for both treatment groups at week 4 (displayed graphically).

Toxicity

	clobetasol propionate shampoo (n = 94)	vehicle (n = 47)	

Proportion of patients with ≥1 study drug related AE	13 (13.8%)	10 (21.3%)	
Skin discomfort which included stinging and burning (this was the most frequently reported dermatologic AE)	10.6%	17%	

- One subject treated with clobetasol propionate shampoo reported conjunctivitis, resolving in one day, not requiring treatment and not causing the patient to discontinue the study
- No case of skin atrophy, telangiectasia, acne, serious adverse events or deaths were reported during the study

Summary

- Results after 4 weeks demonstrated that clobetasol propionate shampoo, 0.05% was with a similar safety profile significantly more effective than its vehicle

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
H. Sofen, C. P. Hudson, F. E. Cook-Bolden, N. Preston, L. E. Colon, S. W. Caveney, and R. W. Gottschalk. Clobetasol propionate 0.05% spray for the manageme	Multicentre (4 centres in the USA) SCALP PSORIASIS DESIGN Between patient Patient delivery	N=81 **Drop-outs (don't complete the study):** N=10 **Clobetasol**: 8 – 4 clear at 2 weeks; 4	**INCLUSION CRITERIA** Aged 18 or over; moderate to severe scalp psoriasis (global severity score 3-4 on a scale of 0-5) **EXCLUSION CRITERIA** Systemic treatment for body psoriasis; >20% BSA psoriasis that required >50g/wk of study product; history of adverse response to topical or systemic steroid therapy; chemical process on the hair within 14 days of baseline visit; use of any of the following within 14	N=41 Clobetasol propionate spray, 0.05% **Formulation**: spray **Frequency:** Twice daily	N=40 Vehicle **Formulation** spray **Frequency:** Twice daily (at least 8	Treatment duration: 4 weeks	**Primary endpoint:** Global severity score (GSS) (6 pt: clear to very severe) at week 4 **Secondar**	Galderma

nt of moderate-to-severe plaque psoriasis of the scalp: Results from a randomized controlled trial. Journal of Drugs in Dermatology 10 (8):885-892, 2011. REF ID: SOFEN2011	ALLOCATION Random Method of randomisation: sequential numbering Concealment: unclear BLINDING Double-blind (patient / investigator) • **Setting:** Not stated • **Washout period**: see exclusion criteria • **Sample size calculation**. Yes. • **ITT analysis** Yes (LOCF)	other **Vehicle**: 2 – 1 adverse event; 1 other	days prior to baseline visit: steroid, UVB, vitamin D3, anthralin, coal tar, any other topical anti-psoriasis medications; anticipated intensive exposure to UV during study period; UVA within 4 weeks, biologics within 12 weeks, systemics within 4 weeks from baseline; women who were pregnant, nursing or planning to become pregnant	(at least 8 hours apart) **Note:** Treatments applied directly onto clean, dry scalp lesions followed by gentle rubbing to ensure a thin film was present on the lesions **Dose:** not to exceed 50g/wk The use of topicals to treat body psoriasis during the course of the study was allowed **Note:** if GSS 0 after 2 weeks subjects completed study at that point	hours apart)		**y endpoints:** GSS at 2 weeks; Skin atrophy	

Demographics

	Clobetasol propionate spray (n =41)	**Vehicle (n=40)**
Mean age (years ±SD)	46.0±15.4	41.3 ±13.7
Male (%)	39%	40%
Race (%)		
Caucasian	78	78
Black/African-American	15	13
Asian	2	5
Native Hawaiian/Pacific Islander	2	0
Other/mixed	2	5
Fitzpatrick skin type (%)		
I	2	5
II	12	20
III	39	38
IV	29	28
V	17	8
VI	0	3

Duration of psoriasis (years)	13.5±12.8	8.6±7.5
GSS		
Moderate	66	70
Severe	34	30

Effect Size

Outcomes

Efficacy

GSS score	**Week 2**		**End of treatment (week 4 or week 2 if GSS = 0 at that time)**	
	Clobetasol propionate (n = 41)	**Vehicle (n = 40)**	**Clobetasol propionate (n = 41)**	**Vehicle (n = 40)**
Clear	5	0	21	1
Almost clear	28	3	14	4
Mild	5	11	4	11
Moderate	2	22	1	18
Severe	1	4	1	6

p-value (between groups)	<0.001	<0.001

Time to max effect

Of those who achieved clear/nearly clear status at week 4, the majority had done so by week 2

Toxicity

	Clobetasol propionate shampoo (n = 41)	**Vehicle (n = 40)**
Skin atrophy	0	1
Withdrawal due to adverse events	0	1

Summary

- Treatment with clobetasol propionate 0.05% spray for up to four weeks is effective and well tolerated for moderate-to-severe plaque psoriasis of the scalp