Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Investigator Global Assessment (IGA) Scale

Score	Grade	Description
0	Clear	Plaque thickening = no elevation or thickening over normal skin Scaling = no evidence of scaling Erythema = none (no residual red coloration but post-inflammatory hyperpigmentation may be present)
1	Almost Clear	Plaque thickening = none or possible thickening but difficult to ascertain if there is a slight elevation above normal skin level Scaling = none or residual surface drying and scaling Erythema = light pink coloration
2	Mild	Plaque thickening = slight but definite elevation Scaling = fine scales partially or mostly covering the lesions Erythema = light red coloration
3	Moderate	Plaque thickening = moderate elevation with rounded or sloped edges Scaling = most lesions at least partially covered Erythema = definite red coloration
4	Severe	Plaque thickening = marked or very marked elevation typically with hard or sharp edges Scaling = non-tenacious or thick tenacious scale, covering most or all of lesions Erythema = very bright red coloration; extreme red coloration; deep red coloration

eTable 2. Other Efficacy Endpoints

	DERMIS-1					DERMIS-2				
Other prespecified efficacy analyses	**Roflumilast Cream 0.3% (n=286)**	**Vehicle Cream (n=153)**	**Difference (95% CI)**	**Odds ratio (95% CI)**	**P value**	**Roflumilast cream 0.3% (n=290)**	**Vehicle Cream (n=152)**	**Difference (95% CI)**	**Odds ratio (95% CI)**	**P value**
IGA Success Week 2, % of patients (95% CI)[a]	5.9 (4, 9) n=269	2.1 (1, 6) n=143	5.4 (1.2, 9.5)	4.42 (1.05, 18.60)	0.06	3.3 (2, 6) n=274	2.1 (1, 6) n=145	1.3 (-1.8, 4.4)	1.75 (0.42, 7.29)	0.92
IGA Success Week 4, % of patients (95% CI)	20.6 (16, 26) n=262	2.3 (1, 6) n=132	19.3 (13.5, 25.1)	13.44 (3.72, 48.58)	<0.001	19.1 (15, 24) n=267	5.8 (3, 11) n=139	13.5 (7.2, 19.9)	3.91 (1.76, 8.70)	0.001
IGA Success Week 6, % of patients (95% CI)	33.3 (28, 39) n=252	6.1 (3, 12) n=131	29.5 (22.1, 36.8)	10.23 (4.18, 25.07)	<0.001	25.6 (21, 31) n=258	4.7 (2, 10) n=129	21.4 (14.5, 28.4)	6.72 (2.82, 16.00)	<0.001
I-IGA Success Week 2, % of patients (95% CI)[b]	34.5 (24, 47) n=58	13.3 (5, 30) n=30	13.3 (-3.0, 29.6)	4.22 (0.52, 34.52)	0.33	34.7 (23, 49) n=49	6.5 (2, 21) n=31	27.0 (8.3, 45.8)	6.18 (1.18, 32.41)	0.03
I-IGA Success Week 4, % of patients (95% CI)	42.3 (30, 56) n=52	27.6 (15, 46) n=29	9.9 (-13.7, 33.6)	1.69 (0.46, 6.22)	0.82	52.1 (38, 66) n=48	17.9 (8, 36) n=28	31.8 (10.1, 53.5)	5.12 (1.40, 18.69)	0.02
I-IGA Success Week 6, % of patients (95% CI)	56.6 (43, 69) n=53	22.2 (11, 41) n=27	41.0 (20.1, 61.8)	10.51 (1.32, 83.49)	0.005	57.8 (43, 71) n=45	13.8 (5, 31) n=29	40.5 (18.7, 62.2)	7.35 (1.97, 27.50)	0.004
I-IGA Clear Week 2, % of patients[c]	20.7 (12, 33) n=58	13.3 (5, 30) n=30	-5.2 (-21.6, 11.2)	0.54 (0.08, 3.69)	0.95	30.6 (20, 45) n=49	3.2 (1, 16) n=31	27.3 (11.8, 42.8)	25.87 (1.41, 475.91)	0.02

I-IGA Clear Week 4, % of patients	28.8 (18, 42) n=52	24.1 (12, 42) n=29	-1.2 (-22.7, 20.2)	0.92 (0.22, 3.81)	0.42	37.5 (25, 52) n=48	10.7 (4, 27) n=28	27.9 (8.2, 47.6)	6.06 (1.28, 28.70)	0.04
I-IGA Clear Week 6, % of patients	49.1 (36, 62) n=53	14.8 (6, 32) n=27	33.6 (12.0, 55.1)	6.48 (1.18, 35.70)	0.03	42.2 (29.9, 57) n=45	10.3 (4, 26) n=29	31.0 (10.3, 51.7)	5.71 (1.35, 24.20)	0.02
WI-NRS Success Week 6, % of patients (95% CI)[d]	57.8 (51, 65) n=192	22.2 (15, 31) n=99	35.4 (24.1, 46.7)	5.28 (2.79, 9.99)	<0.001	62.0 (55, 68) n=205	30.6 (22, 40) n=98	28.3 (16.6, 40.0)	3.43 (1.93, 6.08)	<0.001
PASI-50 Week 2, % of patients (95% CI)[e]	29.9 (25, 36) n=268	10.5 (6, 17) n=143	21.0 (13.6, 28.4)	5.10 (2.45, 10.58)	<0.001	28.7 (24, 34) n=272	6.9 (4, 12) n=145	21.8 (14.6, 29.0)	5.12 (2.52, 10.40)	<0.001
PASI-50 Week 4, % of patients (95% CI)	52.7 (47, 59) n=262	19.7 (14, 27) n=132	36.4 (27.5, 45.2)	5.92 (3.34, 10.49)	<0.001	52.6 (47, 59) n=266	15.8 (11, 23) n=139	33.9 (25.0, 42.7)	5.09 (2.98, 8.70)	<0.001
PASI-50 Week 6, % of patients (95% CI)	67.1 (61, 73) n=252	21.4 (15, 29) n=131	47.5 (38.5, 56.5)	9.13 (4.93, 16.88)	<0.001	63.2 (57, 69) n=258	15.5 (10, 23) n=129	43.1 (34.1, 52.1)	7.87 (4.37, 14.18)	<0.001
PASI-50 Week 8, % of patients (95% CI)	75.3 (70, 80) n=255	26.5 (20, 35) n=132	50.7 (41.3, 60.0)	9.24 (5.13, 16.63)	<0.001	68.9 (63, 74) n=264	24.4 (18, 32) n=131	41.6 (31.9, 51.2)	6.51 (3.73, 11.37)	<0.001
PASI-75 Week 2, % of patients (95% CI)	8.6 (6, 13) n=268	1.4 (0, 5) n=143	7.4 (3.3 11.6)	7.47 (1.64, 34.07)	0.008	2.6 (1, 5) n=272	1.4 (0,5) n=145	1.9 (-1.0, 4.7)	2.57 (0.49, 13.56)	0.52
PASI-75 Week 4 % of patients (95% CI)	21.8 (17, 27) n=262	3.0 (1, 8) n=132	19.0 (13.0, 25.0)	10.44 (3.43, 31.78)	<0.001	16.2 (12, 21) n=266	3.6 (2, 8) n=139	11.8 (6.2, 17.5)	4.57 (1.77, 11.83)	0.002
PASI-75 Week 6 % of patients (95% CI)	31.3 (26, 37) n=252	3.8 (2, 9) n=131	27.8 (21.3, 34.4)	21.72 (5.87, 80.37)	<0.001	28.7 (24, 34) n=258	3.9 (2, 9) n=139	24.2 (17.6, 30.8)	10.96 (3.98, 30.23)	<0.001

PASI-90 Week 2, % of patients (95% CI)	2.2 (1, 5) n=268	0.7 (0, 4) n=143	2.1 (-0.4, 4.7)	4.64 (0.52, 41.56)	0.30	0.7 (0,3) n=272	0 (0, 3) n=145	1.0 (-0.2, 2.2)	NE (NE, NE)	0.4
PASI-90 Week 4 % of patients (95% CI)	6.1 (4, 10) n=262	0.8 (0, 4) n=132	5.5 (2.2, 8.7)	14.87 (1.31,168. 26)	0.02	5.6 (3, 9) n=266	0 (0, 3) n=139	6.1 (3.1, 9.2)	NE (NE, NE)	0.007
PASI-90 Week 6 % of patients (95% CI)	13.1 (9,18) n=252	1.5 (0,5) n=131	12.1 (7.4, 16.8)	21.35 (2.52,180. 81)	<0.001	8.9 (6, 13) n=258	0 (0,3) n=139	9.1 (5.4, 12.8)	NE (NE, NE)	<0.001
PASI-90 Week 8, % of patients (95% CI)	22.4 (18, 28) n=255	2.3 (1, 6) n=132	20.9 (14.9, 26.9)	17.16 (4.25, 69.22)	<0.001	17.0 (13, 22) n=264	2.3 (1, 7) n=131	14.4 (8.8, 19.9)	8.42 (2.45, 28.86)	<0.001
PASI-100 Week 2, % of patients (95% CI)	1.1 (0,3) n=268	0 (0,3) n=143	1.2 (-0.2, 2.6)	NE (NE, NE)	0.41	0 (0, 1) n=272	0 (0, 3) n=145	0 (0, 0)	NE (NE, NE)	NE
PASI-100 Week 4 % of patients (95% CI)	3.8 (2, 7) n=262	0 (0,3) n=132	3.6 (1.1, 6.0)	NE (NE, NE)	0.06	3.4 (2, 6) n=266	0 (0, 3) n=139	3.3 (1,0 5.6)	NE (NE, NE)	0.07
PASI-100 Week 6 % of patients (95% CI)	8.7 (6, 13) n=252	0.8 (0, 4) n=131	7.5 (3.6, 11.3)	17.26 (1.75,170. 10)	0.004	6.6 (4, 10) n=258	0 (0,3) n=139	6.6 (3.4, 9.8)	NE (NE, NE)	0.005
PASI-100 Week 8, % of patients (95% CI)	13.7 (10, 18) n=255	1.5 (0, 5) n=132	12.0 (7.0, 17.0)	10.51 (2.50, 44.14)	<0.001	11.0 (8, 15) n=264	0 (0, 3) n=131	10.9 (6.8, 15.0)	NE (NE, NE)	<0.001

			LS Mean (SE) difference from vehicle (95% CI)					**LS Mean (SE) difference from vehicle (95% CI)**		
Change from Baseline PSD Week 2, LS mean change (95% CI)[f,g]	-34.4 (-38.7, -30.1) n=270	-13.7 (-19.1, -8.4) n=142	-20.7 (-26.1, -15.3)		<0.001	-32.6 (-37.2, -28.0) n=266	-15.6 (-21.2, -10.0) n=141	-17.0 (-22.4, -11.5)		<0.001
Change from Baseline PSD Week 6, LS mean change (95% CI)[g]	-48.0 (-52.6, -43.4) n=251	-17.2 (-23.0, -11.4) n=130	-30.8 (-36.6, -25.0)		<0.001	-46.6 (-51.9, -41.4) n=256	-20.1 (-26.6, -13.6) n=125	-26.6 (-32.9, -20.2)		<0.001

Abbreviations: CfB, change from baseline; CI, confidence interval; IGA, Investigator Global Assessment; I-IGA, intertriginous-Investigator Global Assessment; NE, not estimable; PASI-50, achievement of 50% reduction in Psoriasis Area Severity Index from baseline; PASI-75, achievement of 75% reduction in Psoriasis Area Severity Index from baseline; PASI-90, achievement of 90% reduction in Psoriasis Area Severity Index from baseline; PASI-100, achievement of 100% reduction in Psoriasis Area Severity Index from baseline; PSD, Psoriasis Symptoms Diary; SE, standard error; WI-NRS, Worst Itch-Numeric Rating Scale.

[a] The IGA is a static evaluation of qualitative overall psoriasis severity. IGA Success indicates IGA status of Clear or Almost Clear plus ≥2-grade improvement from baseline assessed on a 5-point scale ranging from 0 (Clear) to 4 (Severe) with higher scores reflecting more severe disease.[11]

[b] I-IGA Success indicates I-IGA status of Clear or Almost Clear plus ≥2-grade improvement from baseline assessed on a 5-point scale ranging from 0 (Clear) to 4 (Severe) with higher scores reflecting more severe disease. Conducted for patients with intertriginous area involvement of at least Mild severity by IGA (I-IGA ≥2) at baseline, evaluating intertriginous areas only and not whole-body involvement

[c] Assessed on a 5-point scale ranging from 0 (Clear) to 4 (Severe) with higher scores reflecting more severe disease. Conducted for patients with intertriginous area involvement of at least Mild severity by IGA (I-IGA ≥2) at baseline, evaluating intertriginous areas only and not whole-body involvement.

[d] The WI-NRS is a simple, single item to assess the patient-reported severity of this symptom at its highest intensity during the previous 24-hour period on a scale from 0 (no itch) to 10 ("worst imaginable itch").[13] Higher scores indicate greater itch. WI-NRS Success indicates ≥4-point reduction on the WI-NRS in patients with WI-NRS score ≥4 at baseline.

[e] PASI combines the assessment of the severity of lesions and the area affected into a single score ranging from 0 (no disease) to 72 (maximal disease) with higher scores reflecting more severe disease.[12]

[f] Patients used the PSD to determine the severity and impact of psoriasis-related signs and symptoms over the past 24 hours. Patients rated each variable in the 16-item assessment on a scale from 0 to 10, with higher scores indicating greater severity or burden.[14]

[g] See eTable 3 in Supplement 5 for additional details.

eTable 3. Summary of Psoriasis Symptoms Diary Total Scores[a]

DERMIS-1	Roflumilast Cream 0.3% (n=286)						Vehicle Cream (n=153)			
	Mean (SD) Score[b]	Change from Baseline, Mean (SD)	Difference from Baseline, LS Mean (95% CI)	P value for Difference from Baseline	Difference from Vehicle, LS Mean (95% CI)	P value for Difference from Vehicle	Mean (SD) Score	Change from Baseline, Mean (SD)	Difference from Baseline, LS Mean (95% CI)	P value for Difference from Baseline
Baseline	72.1 (42.75) n=282						73.4 (41.29) n=150			
Week 2	38.2 (35.28) n=270	-32.9 (32.31) n=270	-34.2 (-38.6, -29.8) n=270	<0.001	-20.1 (-25.6, -14.6)	<0.001	58.0 (39.34) n=142	-15.9 (31.55) n=142	-14.1 (-19.6, -8.7) n=142	<0.001
Week 4	28.9 (32.47) n=261	-41.6 (35.94) n=261	-43.1 (-47.9, -38.3) n=261	<0.001	-24.5 (-30.4, -18.5)	<0.001	53.1 (39.08) n=130	-18.9 (30.97) n=130	-18.6 (-24.5, -12.7) n=130	<0.001
Week 6	24.3 (29.41) n=251	-44.9 (36.16) n=251	-47.1 (-51.8, -42.3) n=251	<0.001	-30.0 (-35.9, -24.0)	<0.001	54.3 (40.49) n=130	-16.8 (36.74) n=130	-17.1 (-23.0, -11.2) n=130	<0.001
Week 8	21.4 (30.04) n=250	-47.7 (38.03) n=250	-49.0 (-53.9, -44.1) n=250	<0.001	-29.6 (-35.8, -23.4)	<0.001	50.0 (40.45) n=129	-21.2 (37.38) n=129	-19.4 (-25.4, -13.4) n=129	<0.001

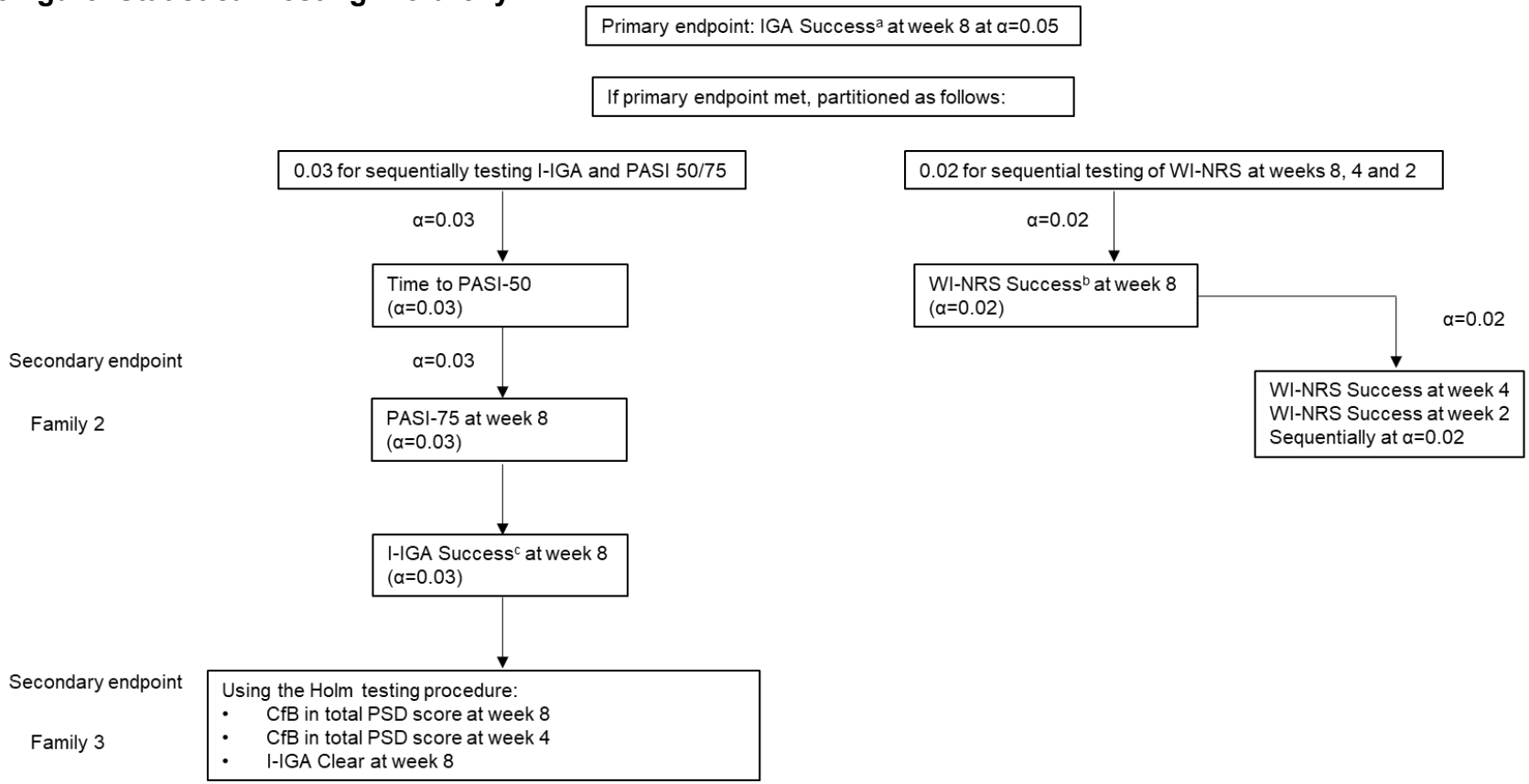
DERMIS-2	Roflumilast cream 0.3% (n=290)						Vehicle Cream (n=152)			
	Mean (SD) Score[b]	Change from Baseline, mean (SD)	Difference from Baseline	P value for Difference from Baseline	Difference from Vehicle	P value for Difference from Vehicle	Mean (SD) Score	Change from Baseline, mean (SD)	Difference from Baseline	P value for Difference from Baseline
Baseline	69.3 (40.66) n=283						77.4 (41.24) n=148			
Week 2	37.1 (35.21) n=266	-31.8 (31.13) n=266	-32.7 (-37.4, -28.0) n=266	<0.001	-17.7 (-23.2, -12.2)	<0.001	59.3 (41.88) n=141	-17.9 (32.28) n=141	-15.0 (-20.7, -9.4) n=141	<0.001
Week 4	27.5 (32.42) n=262	-41.0 (34.39) n=262	-42.5 (-47.6, -37.4) n=262	<0.001	-26.4 (-32.3, -20.4)	<0.001	58.2 (40.78) n=135	-19.1 (33.95) n=135	-16.1 (-22.3, -10.0) n=135	<0.001
Week 6	25.2 (32.26) n=256	-43.5 (35.13) n=256	-47.4 (-52.7, -42.1) n=256	<0.001	-26.8 (-33.0, -20.5)	<0.0001	55.6 (41.67) n=125	-21.4 (38.01) n=125	-20.6 (-27.1, -14.1) n=125	<0.001
Week 8	22.0 (33.25) n=257	-45.9 (35.43) n=257	-49.9 (-55.4, -44.3) n=257	<0.001	-26.8 (-33.3, -20.3)	<0.001	53.6 (44.00) n=127	-23.8 (40.41) n=127	-23.1 (-29.8, -16.3) n=127	<0.001

SD, standard deviation.

[a] Patients used the Psoriasis Symptoms Diary to determine the severity and impact of psoriasis-related signs and symptoms over the past 24 hours. Patients rated each variable in the 16-item assessment on a scale from 0 to 10, with higher scores indicating greater severity or burden.[14]

[b] The mean scores are as observed and the LS mean change from baseline and LS mean change from vehicle, 95% Cis, and P values are from an analysis of covariance (ANCOVA) with treatment, site, baseline Investigator Global Assessment, baseline intertriginous involvement, and baseline Psoriasis Symptoms Diary score as independent variables.

eFigure. Statistical Testing Hierarchy



Abbreviations: CfB, change from baseline; CI, confidence interval; IGA, Investigator Global Assessment; I-IGA, intertriginous-Investigator Global Assessment; PASI-50, achievement of 50% reduction in Psoriasis Area Severity Index from baseline; PASI-75, achievement of 75% reduction in Psoriasis Area Severity Index from baseline; WI-NRS, Worst Itch-Numeric Rating Scale.

[a] The IGA is a static evaluation of qualitative overall psoriasis severity. IGA Success indicates IGA status of Clear or Almost Clear plus ≥2-grade improvement from baseline assessed on a 5-point scale ranging from 0 (Clear) to 4 (Severe) with higher scores reflecting more severe disease.[11]

[b] The WI-NRS is a simple, single item to assess the patient-reported severity of this symptom at its highest intensity during the previous 24-hour period on a scale from 0 (no itch) to 10 ("worst imaginable itch").[13] Higher scores indicate greater itch. WI-NRS Success indicates ≥4-point reduction on the WI-NRS in patients with WI-NRS score ≥4 at baseline.

[c] Conducted for patients with intertriginous area involvement of at least Mild severity by IGA (I-IGA ≥2) at baseline using a 5-point scale ranging from 0 (Clear) to 4 (Severe), evaluating intertriginous areas only and not whole-body involvement. Higher scores indicate more severe disease.