Supplement Table S1: Blinded Investigator Global Assessment of Rosacea Severity Score (IGA-RSS)

Numerical Score	Definition	Description
0	Clear	Almost no Rosacea (i.e. no papules and/or pustules); no or residual erythema; mild to moderate degree of telangiectasia may be present
1	Minimal	Rare papules and/or pustules; residual to mild erythema; mild to moderate degree of telangiectasia may be present
2	Mild	Few papules and/or pustules; mild erythema; mild to moderate degree of telangiectasia may be present
3	Mild to moderate	Distinct number of papules and/or pustules; mild to moderate erythema; mild to moderate degree of telangiectasia may be present
4	Moderate	Pronounced number of papules and/or pustules; moderate erythema; mild to moderate degree of telangiectasia may be present
5	Moderate to Severe	Many papules and/or pustules, occasionally with large inflamed lesions; moderate erythema; moderate degree of telangiectasia may be present
6	Severe	Numerous papules and/or pustules, occasionally with confluent areas of inflamed lesions; moderate to severe erythema; moderate to severe degree of telangiectasia may be present

Supplement Table S2: Schedule of Assessments

Visit Number	Visit 1	Visit 2	Visit 3
Time Point	Week 0 Day 1	Week 2 Day 15	Week 8 Day 57
Informed Consent	X		
Eligibility criteria checked	X		
Demographics and medical history	X		
Randomisation	X		
Administer DLQI	X	X	X
Administer IGA	X	X	X
Participant-rated severity VAS-S completion[a]	X	X	X
Participant-rated change VAS-CS severity completion		X	X
Provision of participant diary	X	X	
Collection of participant diary		X	X
Safety monitoring	X	X	X

DLQI: Dermatology Life Quality Index
IGA-RSS blinded Investigator Global Assessment of Rosacea Severity Score
VAS-S: Participant-rated assessment of severity of rosacea
VAS-CS: Participant-rated assessment of change in severity of rosacea
[a] VAS-S to be completed weekly from Visit 1 until Visit 3, within the subject diary

Supplement Table S3: Clinic-based secondary outcome variables

	Mean (SD)	Median (IQR)	Min to Max
IGA-RSS week Zero			
Control N=69	3 (0.9)	3 (2 to 4)	2 to 5
Honevo® N=68	3 (0.9)	3 (2 to 3.5)	2 to 6
IGA-RSS week 2			
Control N=66	2.5 (1.4)	2 (2 to 3)	0 to 6
Honevo® N=66	2.2 (1.2)	2 (1 to 3)	0 to 6
IGA-RSS week 8			
Control N=54	2.4 (1.3)	2 (1 to 3)	0 to 6
Honevo® N=61	1.8 (1.2)	2 (1 to 3)	0 to 5
Difference IGA-RSS week 2 to week Zero			
Control N=66	-0.5 (0.9)	0 (-1 to 0)	-3 to 1
Honevo® N=66	-0.8 (1.0)	-1 (-2 to 0)	-3 to 2
Difference IGA-RSS week 8 to week Zero			
Control N=54	-0.6 (1.1)	0 (-1 to 0)	-3 to 2
Honevo® N=61	-1.2 (1.1)	-1 (-2 to 0)	-3 to 1
VAS-CS week 2			
Control N=66	50.1 (16.6)	51 (47 to 55)	0 to 89
Honevo® N=66	59.2 (16.1)	59 (50 to 71)	21 to 98
VAS-CS week 8			
Control N=54	55.2 (18.2)	51 (48 to 61)	15 to 98
Honevo® N=61	67.6 (17.4)	69 (52 to 79)	25 to 99
VAS-S week Zero			
Control N=69	32.0 (19.1)	28 (18 to 44)	1 to 87
Honevo® N=68	36.8 (21.2)	31.5 (21 to 54)	1 to 78
VAS-S week 2			
Control N=66	34.9 (19.6)	32.5 (21 to 50)	1 to 84
Honevo® N=66	31.2 (16.9)	29.5 (20 to 42)	1 to 68
VAS-S week 8			
Control N=54	30.8 (19.2)	31 (13 to 46)	3 to 78
Honevo® N=61	26.3 (19.2)	24 (12 to 38)	2 to 96
Difference VAS-S week 2 to week Zero			
Control N=66	3.0 (16.7)	0.5 (-6.0 to 8.0)	-30 to 73
Honevo® N=66	-5.2 (16.1)	-6 (-16 to 1)	-37 to 38
Difference VAS-S week 8 to week Zero			
Control N=54	2.1 (14.5)	-1 (-9 to 11)	-39 to 41
Honevo® N=61	-8.9 (22.4)	-10(-24 to 9)	-66 to 38

IGA-RSS: blinded Investigator Global Assessment of Rosacea Severity Score, based on a 7 point scale (0 ‘clear’ to 6 ‘severe’)
VAS-CS: Participant-rated assessment of Change in Severity of rosacea based on a 100mm VAS scale (0mm ‘much worse’ to 100mm ‘much improved’)
VAS-S: Participant-rated assessment of Severity of rosacea based on a 100mm VAS scale (0mm ‘mildest possible’ symptoms and 100mm ‘worst possible’ symptoms)

Supplement Table S4: Diary-based VAS-S adjusted for baseline

Honevo® minus Control	N with data		Estimate (95% CI)	P
	Honevo®	Control		
VAS-S week 2	52	50	-4.0 (-8.5 to 0.6)	0.088
VAS-S week 3	60	53	-1.3 (-6.8 to 4.2)	0.65
VAS-S week 4	59	54	-4.0 (-10.3 to 2.4)	0.21
VAS-S week 5	55	55	-2.0 (-7.8 to 3.9)	0.50
VAS-S week 6	56	50	-5.3 (-2.5 to 14.2)	0.13
VAS-S week 7	53	50	-2.1 (-8.9 to 4.7)	0.54
VAS-S week 8	48	38	-5.7 (-6.2 to 13.3)	0.15

VAS-S: Participant-rated assessment of Severity of rosacea based on a 100mm VAS scale (0mm 'mildest possible' symptoms and 100mm 'worst possible' symptoms)

Supplement Table S5: Adverse events reported in the Honevo® and Control groups.

	Honevo® N	Control N
Rosacea related adverse events resulting in withdrawal		
Worsening Rosacea	3	8
Rosacea related adverse events without withdrawal		
Worsening Rosacea	0	2
Itching	5	1
Tingling	3	2
Red spots	2	0
Eczema	1	0
Dry skin	1	0
Peeling	1	0
Pain	1	0
Stinging	0	4
Burning	0	2
Blisters	0	1
Bleeding	0	1
Possible fungal skin infection	0	1
Non-rosacea related adverse events resulting in withdrawal		
	0	0
Non-rosacea related adverse events without withdrawal		
Other skin problem	1	0
Infection	6	7
Trauma	3	1
Indigestion	1	0
Worsening Asthma	1	0
Headache / Migraine	1	2
Elevated PSA	1	0
Cardiovascular	0	2
Allergy / Hayfever	0	2

Note: Participants may report more than one adverse event