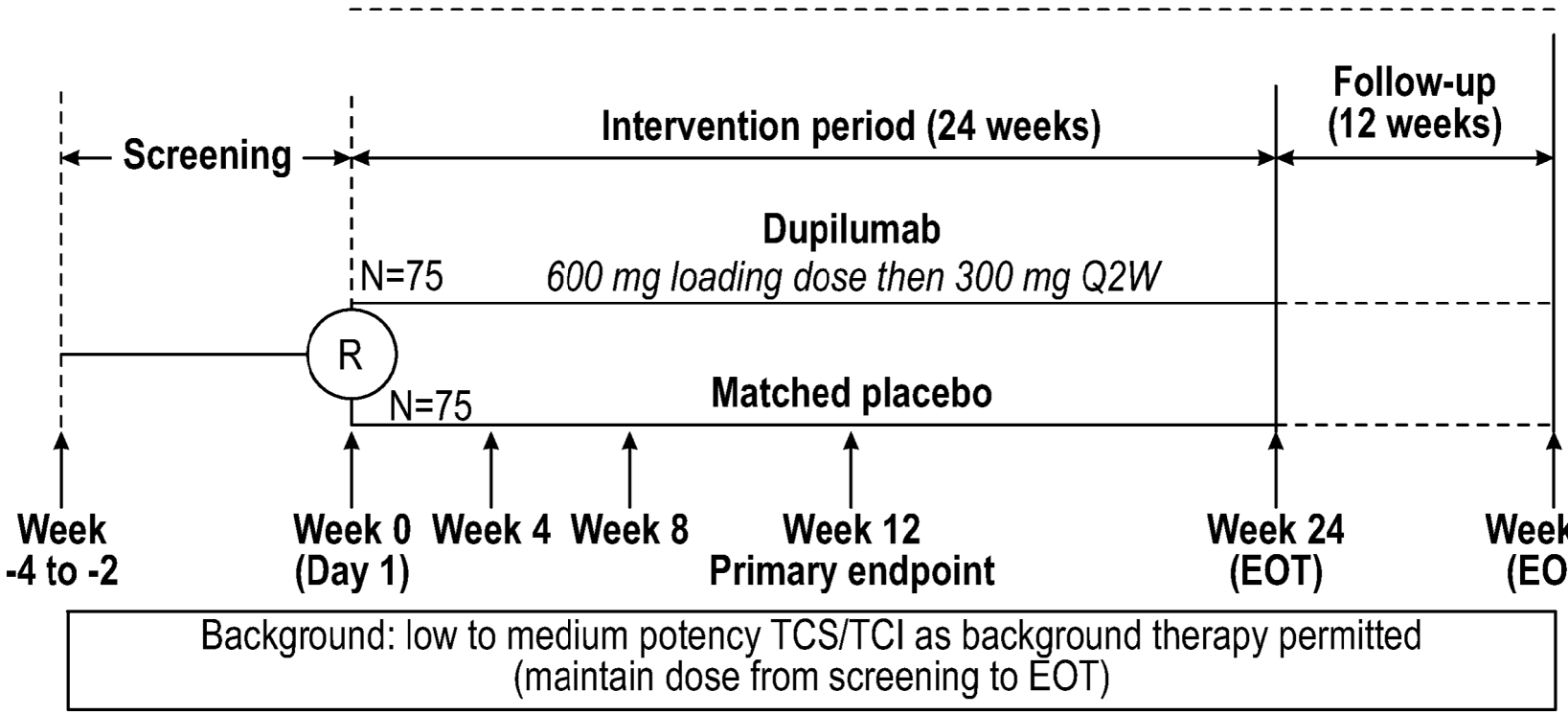


Dupilumab 300 mg Q2W, administered as 1 SC injection of dupilumab 300 mg (2 mL)
A 600 mg loading dose will be administered on Day 1.
Matched placebo is prepared in the same formulation without the addition of protein (ie, the active substance)

EOS: end of study; EOT: end of treatment; PN: prurigo nodularis; Q2W: every 2 weeks; R: randomization; SC: subcutaneous; TCI: topical calcineurin inhibitors; TCS: topical corticosteroids.

FIG. 1

PROCEDURE	SCREENING (2 TO 4 WEEKS BEFORE DAY 1)	INTERVENTION PERIOD (WEEKS)					FOLLOW-UP (12 WEEKS)	NOTES
		0 (DAY 1)	4	8	12	24		
VISIT	1	2[a]	3	4	5	6[b] (EOT)	7 (EOS)	VISIT WINDOW: ±3 DAYS FOR VISITS 3, 4, 5, 6, AND 7.
SCREENING AND BASELINE								
INFORMED CONSENT	X							SEPARATE CONSENT TO BE OBTAINED FOR OPTIONAL PROCEDURES (SKIN BIOPSY, DNA AND RNA SAMPLING, SERUM/ PLASMA SAMPLING FOR ARCHIVAL, AND PHOTOGRAPHY; HIV TEST IF SPECIFIC CONSENT LOCALLY REQUIRED).
MEDICAL HISTORY	X							
PRIOR AND CONCOMITANT MEDICATION	X	X	X	X	X	X	X	CONCOMITANT MEDICATION WILL BE COLLECTED THROUGHOUT THE STUDY.
DEMOGRAPHY	X							
INCLUSION AND EXCLUSION CRITERIA	X	X						
HEPATITIS[C], HIV SEROLOGY, TB TEST	X							HBS AG, HBS AB, HBC AB, HCV AB, HIV SCREEN (ANTI-HIV-1 AND HIV-2 ANTIBODIES), TB TEST (PERFORMED LOCALLY IF REQUIRED AND RESULTS NOTED IN THE ECRF).
RANDOMIZATION		X						
STUDY INTERVENTION[D]								
DISPENSE OR DOWNLOAD E-DIARY	X	X	X	X	X	X	X	DEVICE WILL BE DISPENSED AT SCREENING (INCLUDING INSTRUCTIONS FOR USE). AT EOS, THE E-DIARY WILL BE DOWNLOADED AND RETURNED TO THE SITE.
PARTICIPANT E-DIARY TRAINING	X	X						
CALL IVRS/IWRS	X	X	X	X	X	X	X	AT SCREENING VISIT, IVRS/IWRS WILL BE CALLED AFTER MEDICAL HISTORY CHECK.
IMP ADMINISTRATION		X	X	X	X			IMP ADMINISTRATION Q2W (±3 DAYS) FROM WEEK 0 UNTIL WEEK 22. BETWEEN VISITS, THE PARTICIPANTS WILL SELF-INJECT IMP AT HOME OR MAY CHOOSE TO HAVE INJECTIONS ADMINISTERED AT HOME BY A CAREGIVER OR AT THE STUDY SITE.

FIG. 2A

PROCEDURE	SCREENING (2 TO 4 WEEKS BEFORE DAY 1)	INTERVENTION PERIOD (WEEKS)					FOLLOW-UP (12 WEEKS)	NOTES
		0 (DAY 1)	4	8	12	24		
VISIT	1	2[a]	3	4	5	6[b] (EOT)	7 (EOS)	VISIT WINDOW: ±3 DAYS FOR VISITS 3, 4, 5, 6, AND 7.
SAFETY[d]								
PHYSICAL EXAMINATION	X	X				X	X	INCLUDING SKIN (FULL BODY SKIN EXAM), NASAL CAVITIES, EYES, EARS, RESPIRATORY, CARDIOVASCULAR, GASTROINTESTINAL, NEUROLOGICAL, LYMPHATIC, AND MUSCULOSKELETAL SYSTEMS.
VITAL SIGNS	X	X	X	X	X	X	X	INCLUDING SBP AND DBP (MMHG), PULSE RATE (BEATS PER MINUTE), BODY TEMPERATURE (°C), AND RESPIRATORY RATE. BODY WEIGHT WILL BE RECORDED AT VISITS 1, 6, AND 7 ONLY. HEIGHT WILL BE RECORDED AT VISIT 1 ONLY.
12-LEAD ECG	X					X		LOCALLY COLLECTED AND READ.
HEMATOLOGY, BIOCHEMISTRY[e]	X	X	X	X	X	X	X	INCLUDING HEMOGLOBIN, HEMATOCRIT, PLATELET COUNT, TOTAL WBC COUNT, DIFFERENTIAL COUNT, TOTAL RBC COUNT, CREATININE, BUN, GLUCOSE, LACTATE DEHYDROGENASE, URIC ACID, TOTAL CHOLESTEROL, TOTAL PROTEIN, ALBUMIN, TOTAL BILIRUBIN, ALT, AST, ALKALINE PHOSPHATASE, ELECTROLYTES (SODIUM, POTASSIUM, CHLORIDE), BICARBONATE, CREATINE PHOSPHOKINASE, AND HEMOGLOBIN A1C (ONLY FOR DIABETIC PATIENTS WITHOUT HEMOGLOBIN A1C LABORATORY RESULTS WITHIN 3 MONTHS BEFORE SCREENING VISIT).
URINALYSIS	X	X	X	X	X	X		DIPSTICK ANALYSIS INCLUDING SPECIFIC GRAVITY, PH, GLUCOSE, KETONES, BLOOD, PROTEIN, NITRITE, LEUKOCYTE ESTERASE, UROBILINOGEN AND BILIRUBIN. IF POSITIVE FOR PROTEIN AND/OR RED BLOOD CELLS, MICROSCOPIC ANALYSIS WILL BE PERFORMED BY THE CENTRAL LABORATORY. CREATININE, LEUKOTRIENE AND TETRANOR PGDM WILL BE TESTED BY THE CENTRAL LABORATORY. URINE SAMPLE HAS TO BE COLLECTED AT THE SAME TIME (±1 HOUR) ESTABLISHED AT V2 IN A GIVEN PATIENT, IF POSSIBLE.
CD4 T CELL COUNT AND HIV VIRAL LOAD	X					X		FOR PARTICIPANTS WITH HIV HISTORY ONLY.
PREGNANCY TEST (WOCBP ONLY)[g]	SERUM	URINE	URINE	URINE	URINE	URINE	URINE	IN BETWEEN VISIT URINE PREGNANCY TEST WILL BE PERFOMED AT HOME (WEEKS 16, 20, 28, 32).
AE REPORTING, INCLUDING SAES	X	X	X	X	X	X	X	

FIG. 2B

PROCEDURE	SCREENING (2 TO 4 WEEKS BEFORE DAY 1)	INTERVENTION PERIOD (WEEKS)					FOLLOW-UP (12 WEEKS)	NOTES
		0 (DAY 1)	4	8	12	24		
VISIT	1	2[a]	3	4	5	6[b] (EOT)	7 (EOS)	VISIT WINDOW: ±3 DAYS FOR VISITS 3, 4, 5, 6, AND 7.
RESCUE MEDICATION USE		←– – – – – – – – – – – – – – – – →						
PK AND ADA[d,f]								
SERUM PK SAMPLES FOR DUPILUMAB CONCENTRATION		X	X	X	X	X	X	
ANTI-DUPILUMAB ANTIBODY		X			X	X	X	
BIOMARKERS[d]								
TOTAL SERUM LGE		X	X	X	X	X	X	
OPTIONAL SKIN BIOPSY (SUBSTUDY)		X				X		THE SAMPLE WILL BE TAKEN FROM LESION AND NON-LESION SKIN USING PUNCH BIOPSY.
OPTIONAL SERUM/PLASMA FOR ARCHIVAL SAMPLES		X	X	X	X	X	X	ARCHIVE SERUM AND PLASMA SAMPLES WILL BE COLLECTED AND STORED FOR POSSIBLE FUTURE ANALYSIS OF POTENTIAL BIOMARKERS OF DRUG RESPONSE, DISEASE ACTIVITY, SAFETY, AND THE TYPE 2 INFLAMMATION PATHWAY.
OPTIONAL DNA (WHOLE BLOOD)SAMPLE[h]		X						
OPTIONAL RNA (WHOLE BLOOD) SAMPLE[h]		X				X		
EFFICACY[d]								
WI-NRS	NRS: ONCE A DAY FROM SCREENING TO EOS							TO BE RECORDED ONCE A DAY IN E-DIARY.
PAIN-NRS								
SLEEP-NRS								

FIG. 2C

PROCEDURE	SCREENING (2 TO 4 WEEKS BEFORE DAY 1)	INTERVENTION PERIOD (WEEKS)					FOLLOW-UP (12 WEEKS)	NOTES
		0 (DAY 1)	4	8	12	24		
VISIT	1	2[a]	3	4	5	6[b] (EOT)	7 (EOS)	VISIT WINDOW: ±3 DAYS FOR VISITS 3, 4, 5, 6, AND 7.
DLQI		X	X	X	X	X	X	ENTERED BY PARTICIPANT DURING SITE VISIT ON A TABLE PROVIDED TO THE SITE.
HADS		X			X	X	X	
EQ-5D-5L		X			X	X	X	
PGIS	X	X	X	X	X	X		
PGIC			X	X	X	X		
MISSED SCHOOL/WORK DAYS (BASELINE VERSION)		X						
MISSED SCHOOL/WORK DAYS(POSTBASELINE VERSION)					X	X	X	
MODIFIED PAS (SCREENING-BASELINE VERSION)	X	X						INVESTIGATOR'S ASSESSEMENT TO BE ENTERED ON A TABLE PROVIDED TO THE SITE.
MODIFIED PAS (FOLLOW-UP VERSION)			X	X	X	X	X	
IGA PN-A AND IGA PN-S		X	X	X	X	X	X	
OPTIONAL PHOTOGRAPHY (SUBSTUDY)		X	X	X	X	X	X	

FIG. 2D

Worst-itch NRS

On a scale from 0 (no itch) to 10 (worst imaginable itch), how was your worst itch in the past 24 hours? Please select one number.

0	1	2	3	4	5	6	7	8	9	10

FIG. 3

IGA Nodular Prurigo

Version 2.0 (December 06 2018)

Score	Category	Description: Activity (IGA PN-A)
0	Clear	No nodules have excoriations or crusts
1	Almost Clear	Very small proportion of nodules have excoriations or crusts (up to approximately 10% of all nodules)
2	Mild	Minority of nodules have excoriations or crusts (approximately 11-25% of all nodules)
3	Moderate	Many nodules have excoriations or crusts (approximately 26-75% of all nodules)
4	Severe	Majority of nodules have excoriations or crusts (approximately 76-100% of all nodules)

Score	Category	Description: Stage (IGA PN-S)
0	Clear	No nodules (0 nodules)
1	Almost Clear	Rare palpable pruriginous nodules (approximately 1-5 nodules)
2	Mild	Few palpable pruriginous nodules (approximately 6-19 nodules)
3	Moderate	Many palpable pruriginous nodules (approximately 20-100 nodules)
4	Severe	Abundant palpable pruriginous nodules (over 100 nodules)

FIG. 4

Prurigo Activity Score (PAS) Name:_____ Date:_____
[DD/MM/YYYY]

1a. Type of Prurigo: Which lesions do you see? (Multiple answers possible)

- ☐ Hypo-/Hyperpigmented maculae
- ☐ Papules
- ☐ Nodules
- ☐ Plaques
- ☐ Ulcers

1b. Type of Prurigo: Which type of prurigo is predominant? (Single answer only)

- ☐ Completely healed (except scars)
- ☐ Prurigo papular type
- ☐ Prurigo nodular type
- ☐ Prurigo plaques type
- ☐ Prurigo ulcerated type

2. Number: How many prurigo lesions do you see? (Single answer only)

- ☐ 0
- ☐ 1-19
- ☐ 20-100
- ☐ >100

Please note
Estimate, do not count!
Do not consider scars.

3. Distribution: Please mark the affected area(s) (Multiple selection possible)

Area	Affected (Please mark as appropriate)	Code for item 4
Left forearm	( )	(1)
Right forearm	( )	(2)
Upper left arm	( )	(3)
Upper right arm	( )	(4)
Lower left leg	( )	(5)
Lower right leg	( )	(6)
Upper left leg	( )	(7)
Upper right leg	( )	(8)
Ventral trunk (see Fig. 1)	( )	(9)
Dorsal trunk (see Fig. 1)	( )	(10)
Capillitium	( )	(11)
Face	( )	(12)

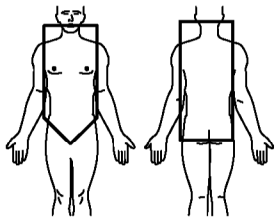


FIG. 1

4. Representative Area:

FIG. 5

Please choose a representative area which will be re-examined during each visit. During the study the area must be always the same, please count in that area!

Representative area (see Code from item 3): ——

Exact number of pruriginous lesions in representative area (exduding scars): ——

5. Activity: Please mark the respective percentage in comparison to all pruriginous lesions.

(Single answer only)

a) Pruriginous lesions with excoriations/crusts:	0%	1-25%	26-50%	51-75%	76-100%
b) Healed prurigo lesions:	100%	75-99%	50-74%	25-49%	0-24%

FIG. 5 (Continued)

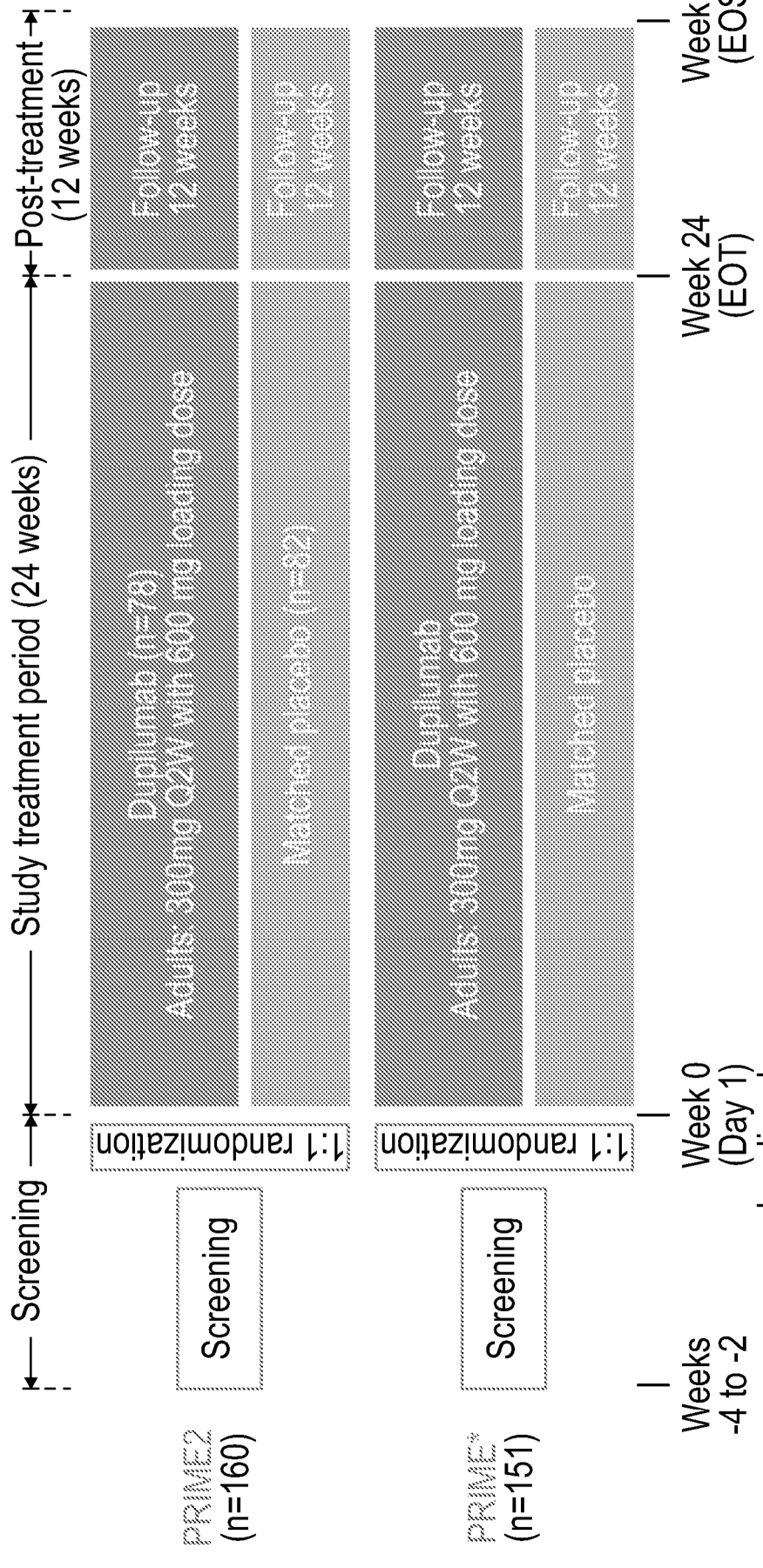

Screening
Study treatment period (24 weeks)
Post-treatment (12 weeks)
PRIME2 (n=160)
Screening
1:1 randomization
Dupilumab (n=78) Adults: 300mg Q2W with 600 mg loading dose
Matched placebo (n=82)
Follow-up 12 weeks
Follow-up 12 weeks
PRIME* (n=151)
Screening
1:1 randomization
Dupilumab Adults: 300mg Q2W with 600 mg loading dose
Matched placebo
Follow-up 12 weeks
Follow-up 12 weeks
Weeks -4 to -2
Week 0 (Day 1) Loading dose administered
Week 24 (EOT)
Week 36 (EOS)

FIG. 6

Endpoint	Definition	Timepoint (week)	Placebo[a] N=76 (SD or %)	Dupilumab[a] N=75 (SD or %)	Dupi vs. Pbo (95% CI)[b]	P-value	US hierarchy	Ex-US hierarchy
WI-NRS>=4 Range 0-10, high worse	**% of patients (itch)**	**24**	**14 (18.4%)**	**45 (60.0%)**	**OR: 6.5 (2.78, 15.41) Model*: 42.7% (27.76%, 57.72%) Tx diff: 41.6%**	**<0.0001**	**1-Primary**	**1-Primary**
IGA PN-S (0/1) Range 0-4, high worse	% of patients (lesions)	24	14 (18.4%)	36 (48.0%)	OR: 4.0 (1.81, 8.98) Model*: 28.3% (13.41%, 43.16%) Tx diff: 29.6%	0.0004	2-Key 2nd	2-Key 2nd
WI-NRS>=4 & IGA PN-S (0/1)	% of pts (itch & lesions)	24	7 (9.2%)	29 (38.7%)	OR: 6.9 (2.49, 19.05) Model*: 29.6% (16.42%, 42.81%) Tx diff: 29.5%	<0.0001	3-Key 2nd	n/a
WI-NRS (itch)	%Δ from BL	24	-22.22 (5.74)	-48.89 (5.61)	-26.67 (-38.44, -14.90)	<0.0001	4	3
DLQI (dermQoL) Range 0-30, high worse	Δ from BL	24	-5.77 (1.05)	-11.97 (1.02)	-6.19 (-8.34, -4.05)	<0.0001	5	4
Skin Pain-NRS Range 0-10, high worse	Δ from BL	24	-2.16 (0.44)	-4.33 (0.43)	-2.17 (-3.07, -1.28)	<0.0001	6	5
HADS Range 0-42, high worse	Δ from BL	24	-2.02 (0.94)	-4.62 (0.93)	-2.60 (-4.52, -0.67)	0.0082	7	6

FIG. 7A

Endpoint	Definition	Timepoint (week)	Placebo[4] N=82 (SD or %)	Dupilumab[4] N=78 (SD or %)	Dupi vs. Pbo (95% CI)[6]	P-value	US hierarchy	Ex-US hierarchy
WI-NRS>=4	% of patients (itch)	12	18 (22.0%)	29 (37.2%)	OR: 2.3 (1.08, 5.00) Model*: 16.8% (2.34%, 31.16%) *Tx diff: 15.2%*	0.0216	1-Primary	1-Primary
WI-NRS>=4	% of patients (itch)	24	16 (19.5%)	45 (57.7%)	OR: 9.0 (3.56, 22.66) Model*: 42.6% (29.06%, 56.08%) *Tx diff: 38.2%*	<0.0001	2-Key 2nd	2-Key 2nd
IGA PN-S (0/1)	% of patients (lesions)	24	13 (15.9%)	35 (44.9%)	OR: 4.4 (2.02, 9.55) Model*: 30.8% (16.37%, 45.22%) *Tx diff: 29%*	<0.0001	3-Key 2nd	3-Key 2nd
WI-NRS>=4 & IGA PN-S (0/1)	% of pts (itch & lesions)	24	7 (8.5%)	25 (32.1%)	OR: 6.1 (2.03, 18.11) Model*: 25.5% (13.9%, 37.86%) *Tx diff: 23.6%*	0.0001	4-Key 2nd	n/a
IGA PN-S (0/1)	% of patients (lesions)	12	10 (12.2%)	20 (25.6%)	OR: 2.9 (1.13, 7.52) Model*: 14.8% (2.64%, 26.99%) *Tx diff: 13.4%*	0.0194	5	5
WI-NRS (itch)	%Δ from BL	24	-36.18 (6.21)	-59.34 (6.39)	-23.16 (-33.81, -12.51)	<0.0001	6	4
DLQI (derm QoL)	Δ from BL	24	-6.77 (1.18)	-13.16 (1.21)	-6.39 (-8.42, -4.36)	<0.0001	7	6
Skin Pain-NRS	Δ from BL	24	-2.74 (0.51)	-4.35 (0.53)	-1.61 (-2.49, -0.73)	0.0003	8	7
Sleep-NRS	Δ from BL	24	0.76 (0.45)	1.30 (0.46)	0.54 (-0.22, 1.30)	**0.1658**	9	8
HADS	Δ from BL	24	-2.59 (1.03)	-5.55 (1.06)	-2.96 (-4.73, -1.19)	0.0010	10	9

FIG. 7B

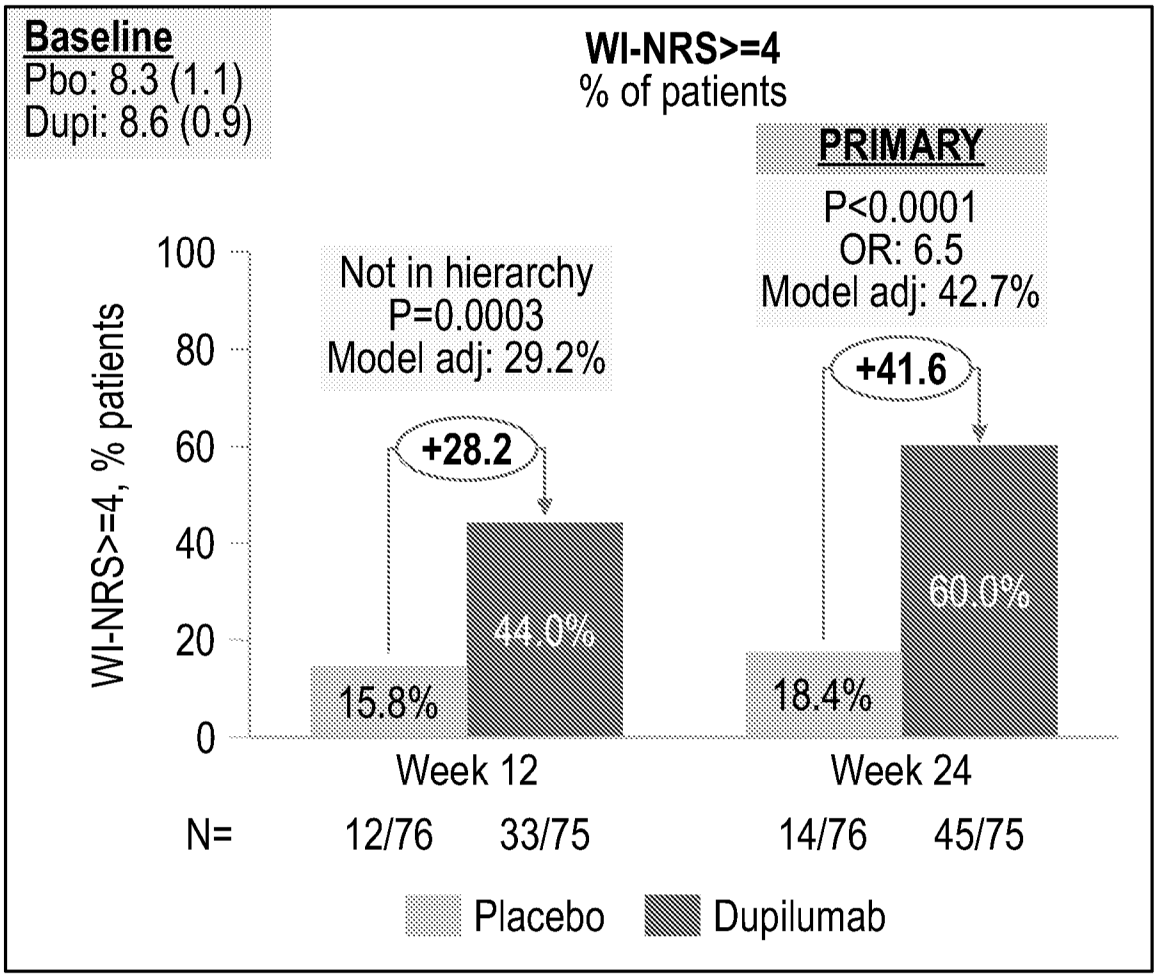

Baseline
Pbo: 8.3 (1.1)
Dupi: 8.6 (0.9)
WI-NRS>=4
% of patients
PRIMARY
P<0.0001
OR: 6.5
Model adj: 42.7%
Not in hierarchy
P=0.0003
Model adj: 29.2%
+28.2
+41.6
WI-NRS>=4, % patients
100
80
60
40
20
0
15.8%
44.0%
18.4%
60.0%
Week 12
Week 24
N=
12/76
33/75
14/76
45/75
Placebo
Dupilumab

FIG. 8A

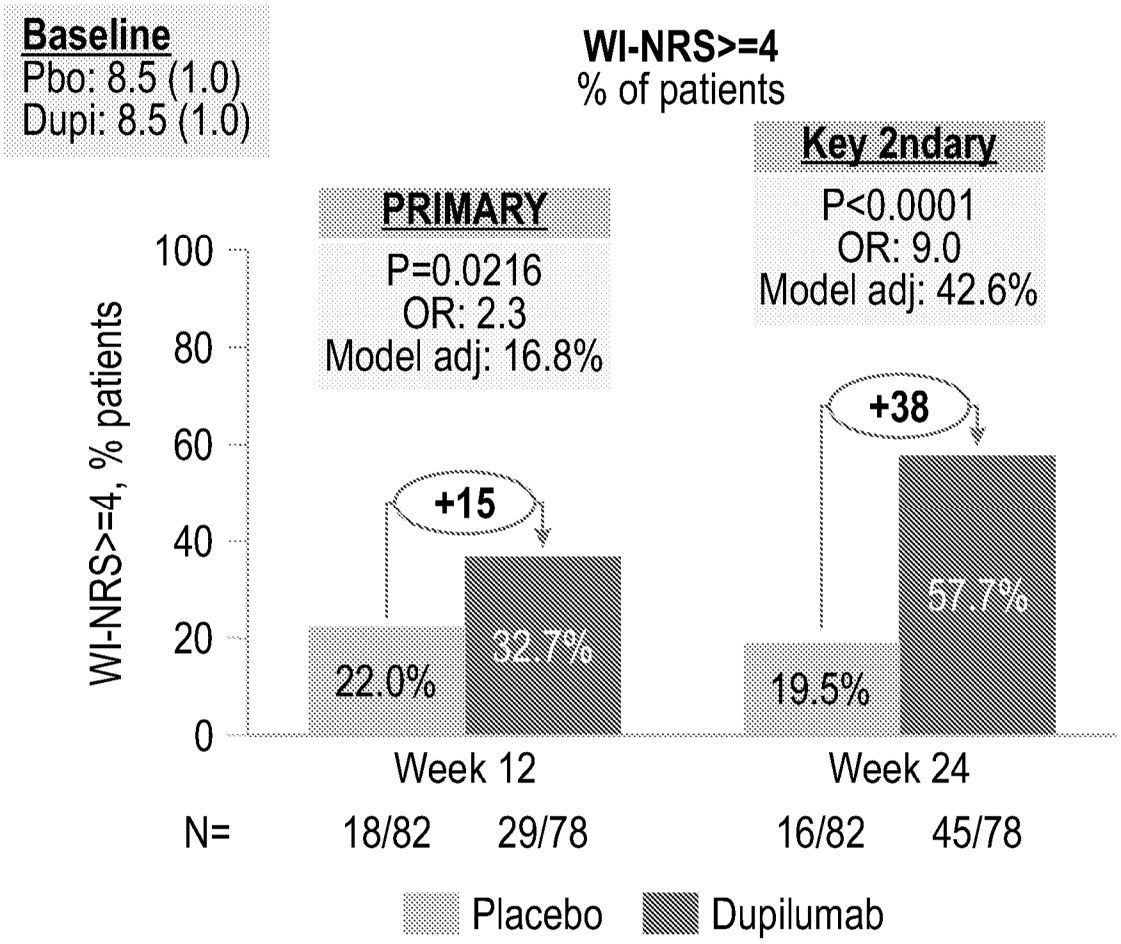
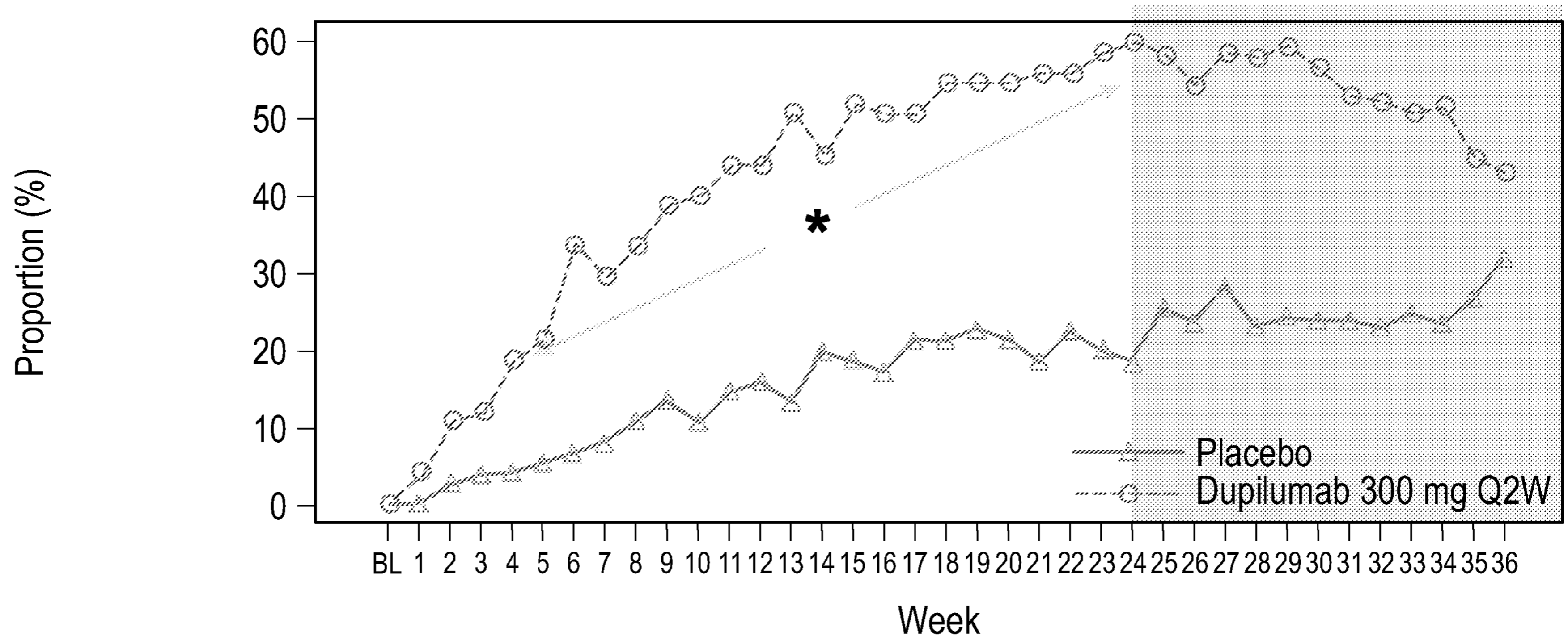

Baseline
Pbo: 8.5 (1.0)
Dupi: 8.5 (1.0)
WI-NRS>=4
% of patients
PRIMARY
P=0.0216
OR: 2.3
Model adj: 16.8%
Key 2ndary
P<0.0001
OR: 9.0
Model adj: 42.6%
WI-NRS>=4, % patients
100
80
60
40
20
0
+15
+38
22.0%
32.7%
19.5%
57.7%
Week 12
Week 24
N=
18/82
29/78
16/82
45/78
Placebo
Dupilumab

FIG. 8B

* p-value<0.05

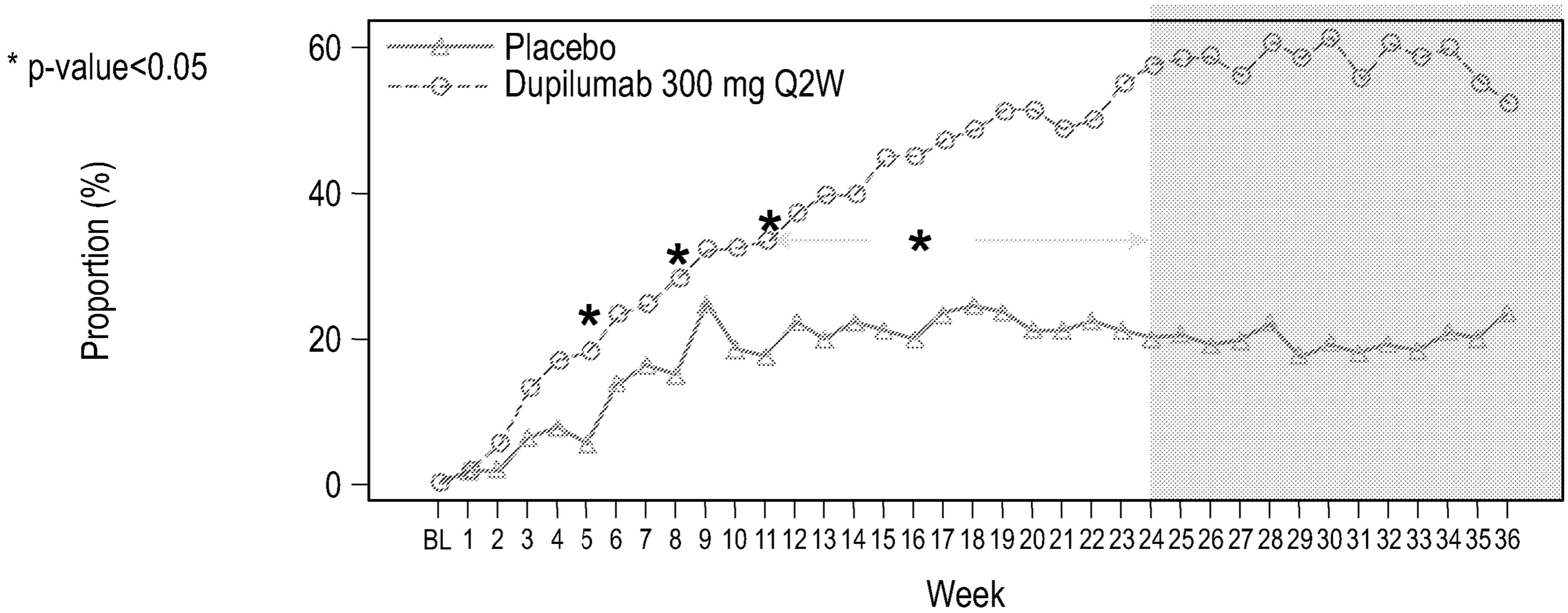
Figure of proportion of participants with WI-NRS improvement (reduction) from baseline >=4 points over time up to Week 36-ITT population



#Participants

Placebo	76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 76 67 64 61 61 58 59 59 57 57 56 53 54
Dupilumab 300 mg Q2W	75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 75 72 70 70 69 69 69 68 67 65 64 60 56

FIG. 8C



#Participants

Placebo 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 82 70 70 62 60 58 53 51 48 45 44 41 39

Dupilumab 300 mg Q2W 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 78 70 68 66 61 58 57 54 51 51 50 49 46

FIG. 8D

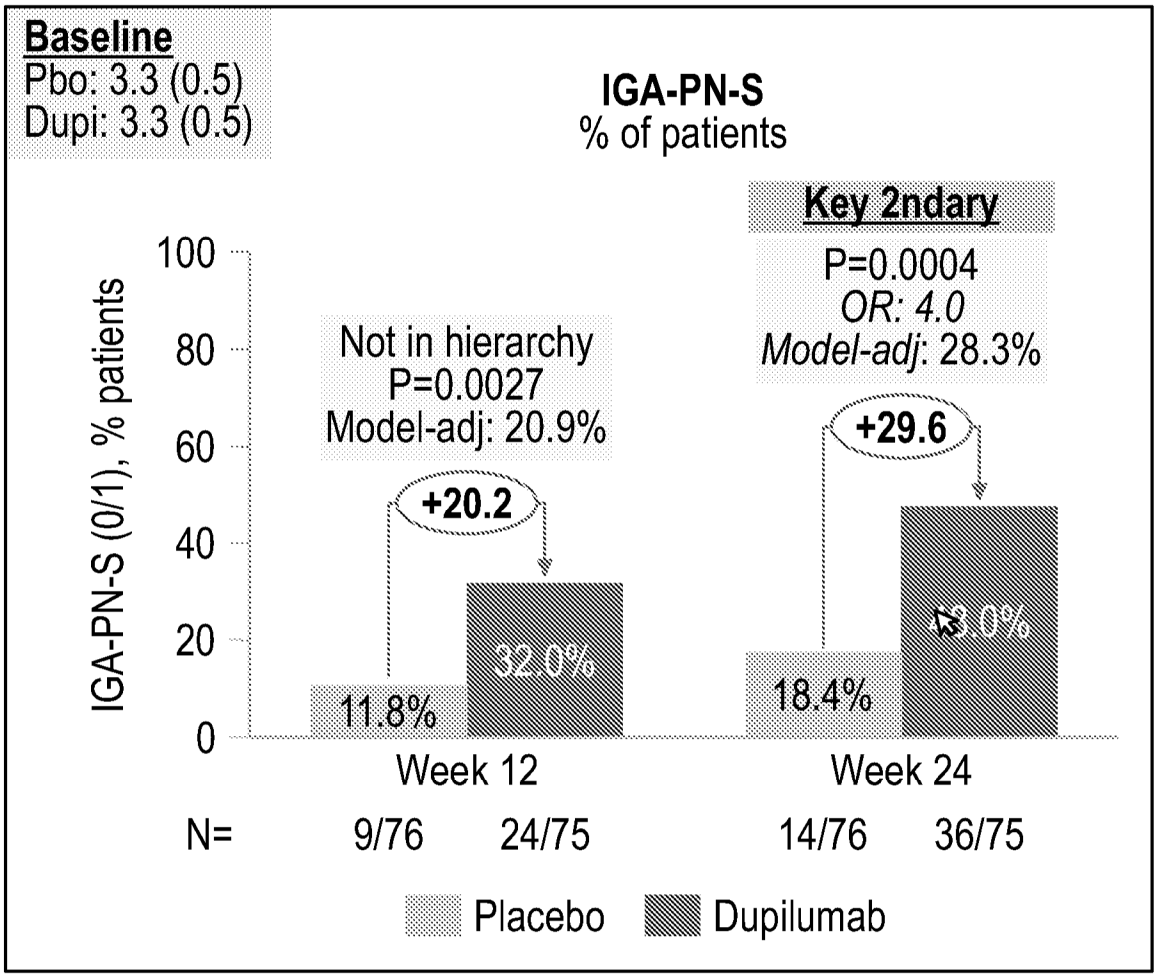

Baseline
Pbo: 3.3 (0.5)
Dupi: 3.3 (0.5)
IGA-PN-S
% of patients
Key 2ndary
P=0.0004
OR: 4.0
Model-adj: 28.3%
Not in hierarchy
P=0.0027
Model-adj: 20.9%
+29.6
+20.2
IGA-PN-S (0/1), % patients
100
80
60
40
20
0
11.8%
32.0%
18.4%
43.0%
Week 12
Week 24
N=
9/76
24/75
14/76
36/75
Placebo
Dupilumab

FIG. 9A

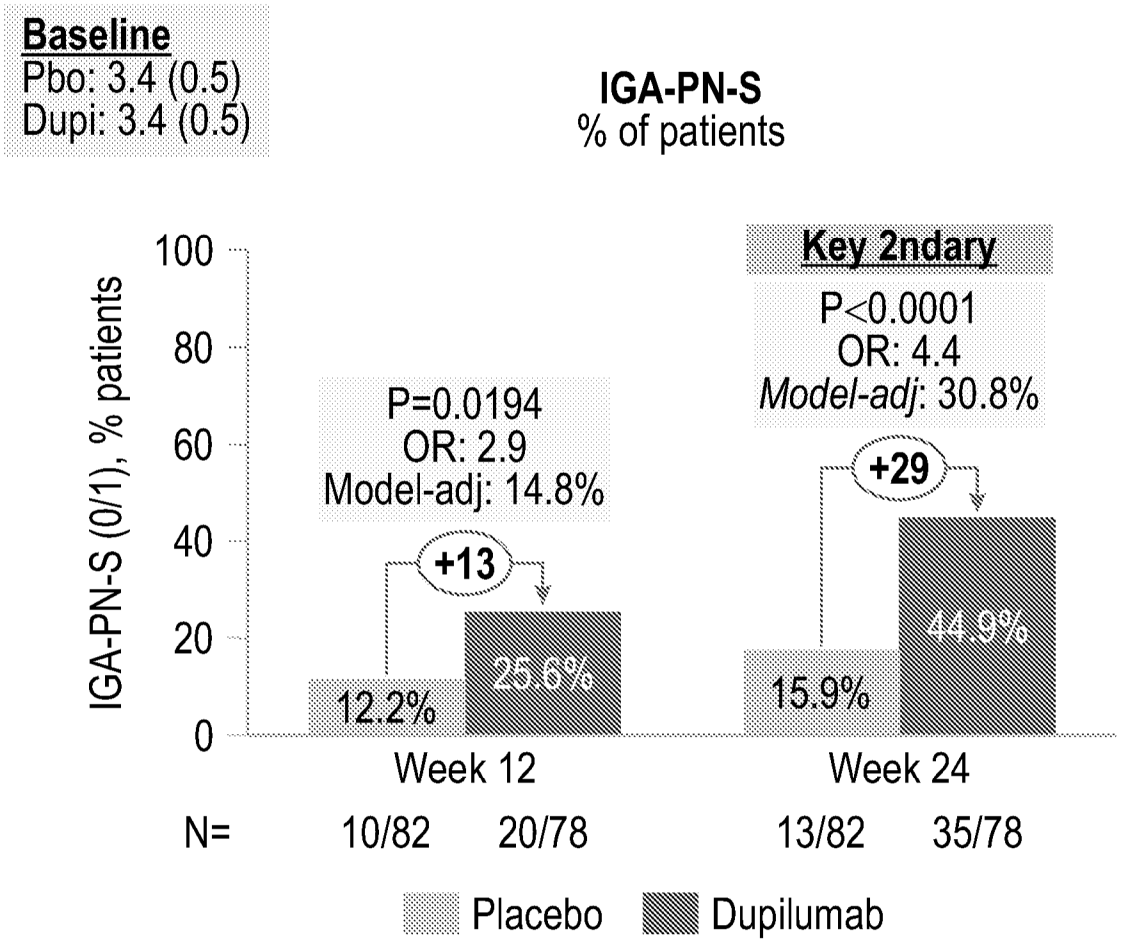

Baseline
Pbo: 3.4 (0.5)
Dupi: 3.4 (0.5)
IGA-PN-S
% of patients
IGA-PN-S (0/1), % patients
100
80
60
40
20
0
P=0.0194
OR: 2.9
Model-adj: 14.8%
+13
12.2%
25.6%
Key 2ndary
P<0.0001
OR: 4.4
Model-adj: 30.8%
+29
15.9%
44.9%
Week 12
Week 24
N=
10/82
20/78
13/82
35/78
Placebo
Dupilumab

FIG. 9B

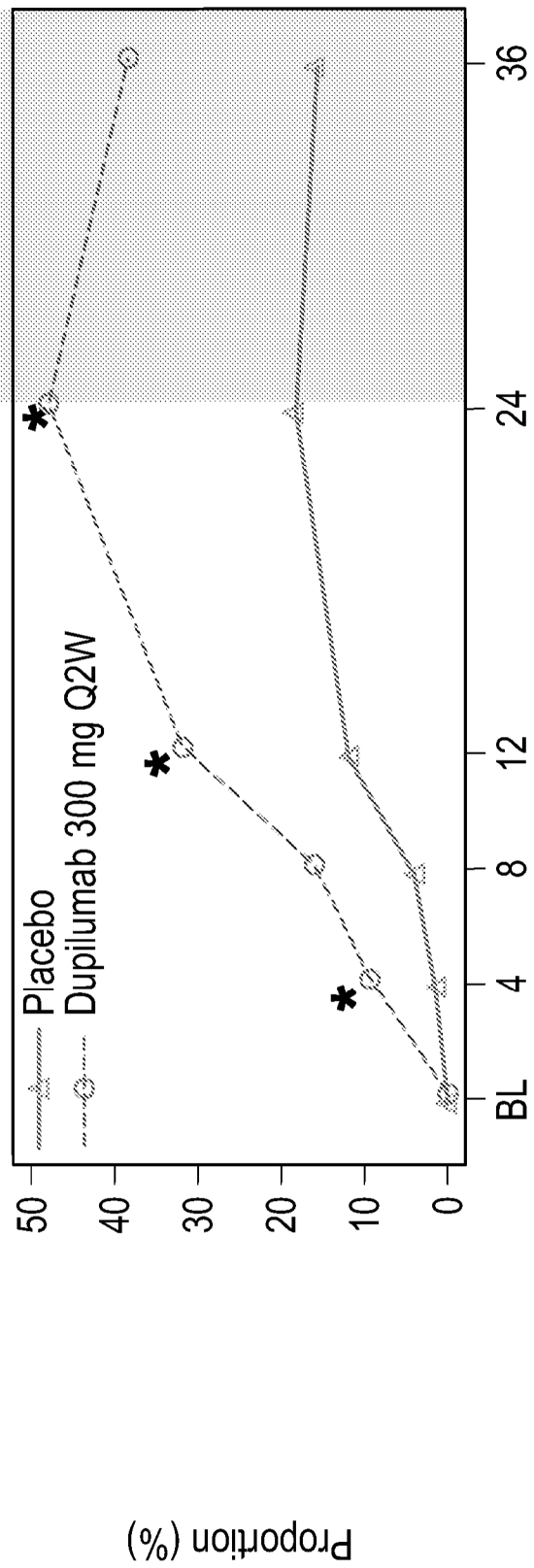
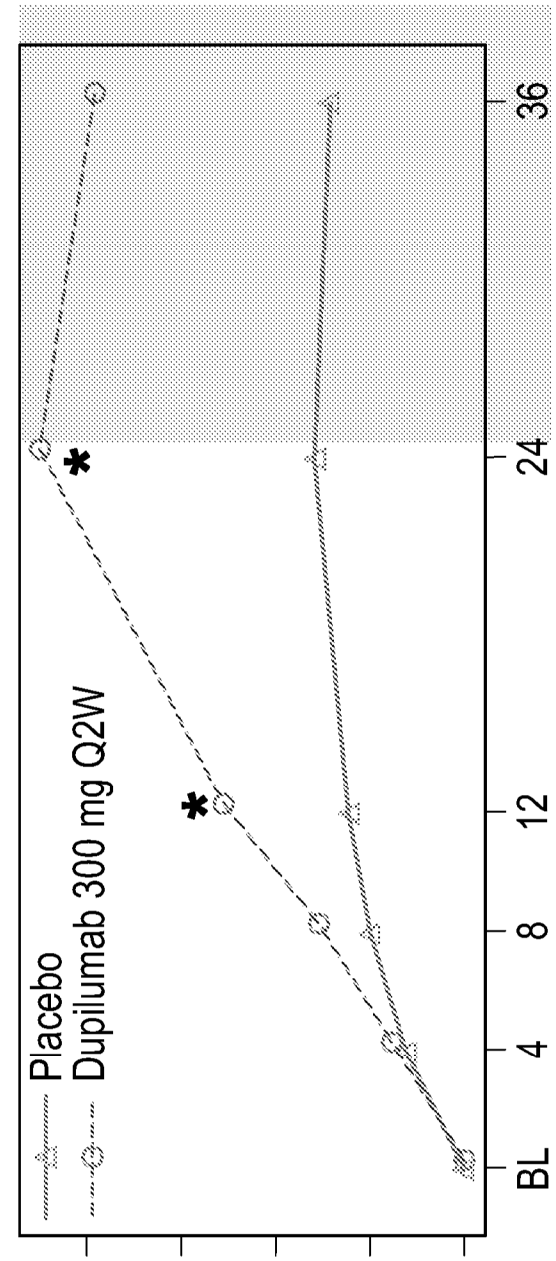

Placebo
Dupilumab 300 mg Q2W
Proportion (%)
50
40
30
20
10
0
*
*
*
BL
4
8
12
24
36
Week
#Participants
Placebo 76 76 76 76 76 57
Dupilumab 300 mg Q2W 75 75 75 75 75 62

FIG. 9C



#Participants

Placebo	82	82	82	82	82	42
Dupilumab 300 mg Q2W	78	78	78	78	78	46

FIG. 9D

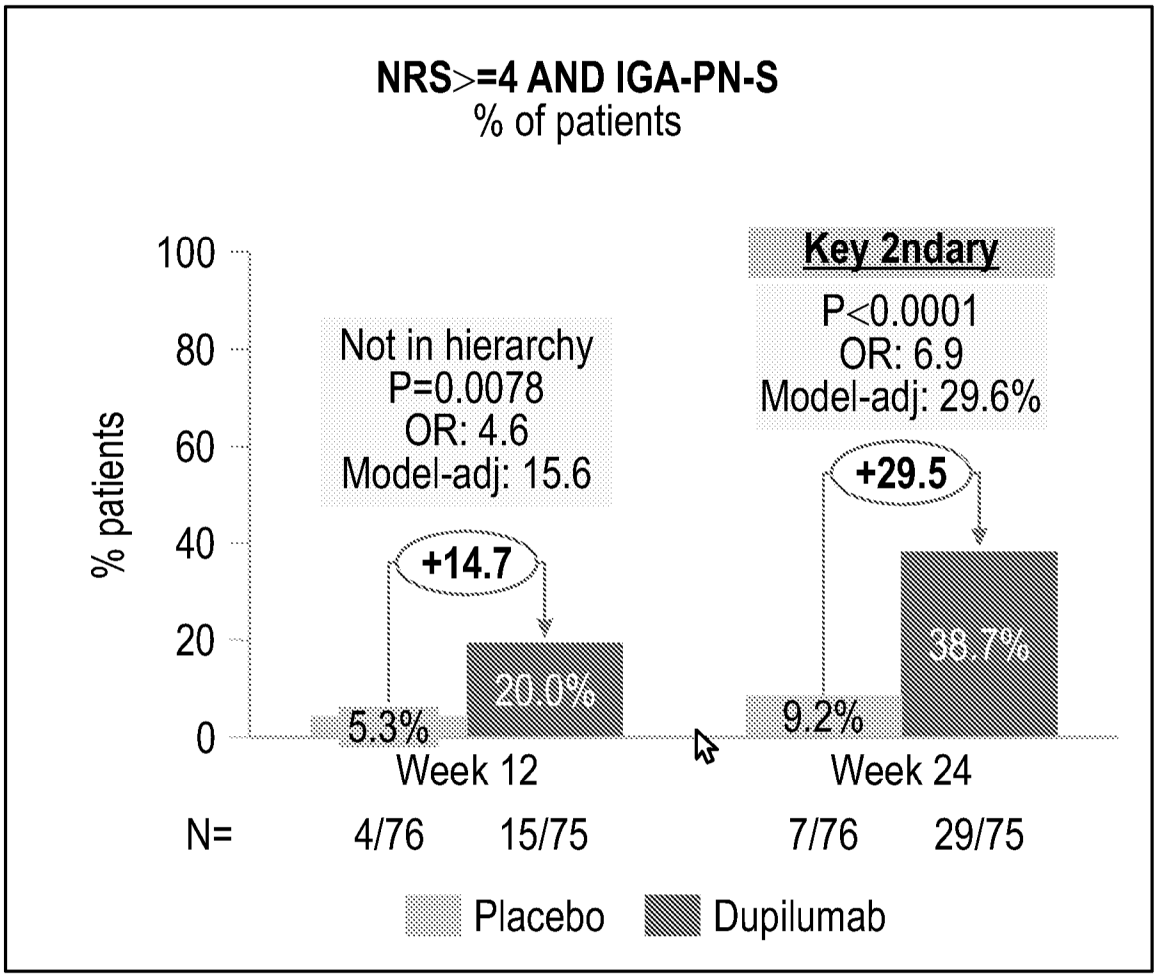

NRS>=4 AND IGA-PN-S
% of patients
% patients
100
80
60
40
20
0
Not in hierarchy
P=0.0078
OR: 4.6
Model-adj: 15.6
Key 2ndary
P<0.0001
OR: 6.9
Model-adj: 29.6%
+14.7
+29.5
5.3%
20.0%
9.2%
38.7%
Week 12
Week 24
N=
4/76
15/75
7/76
29/75
Placebo
Dupilumab

FIG. 10A

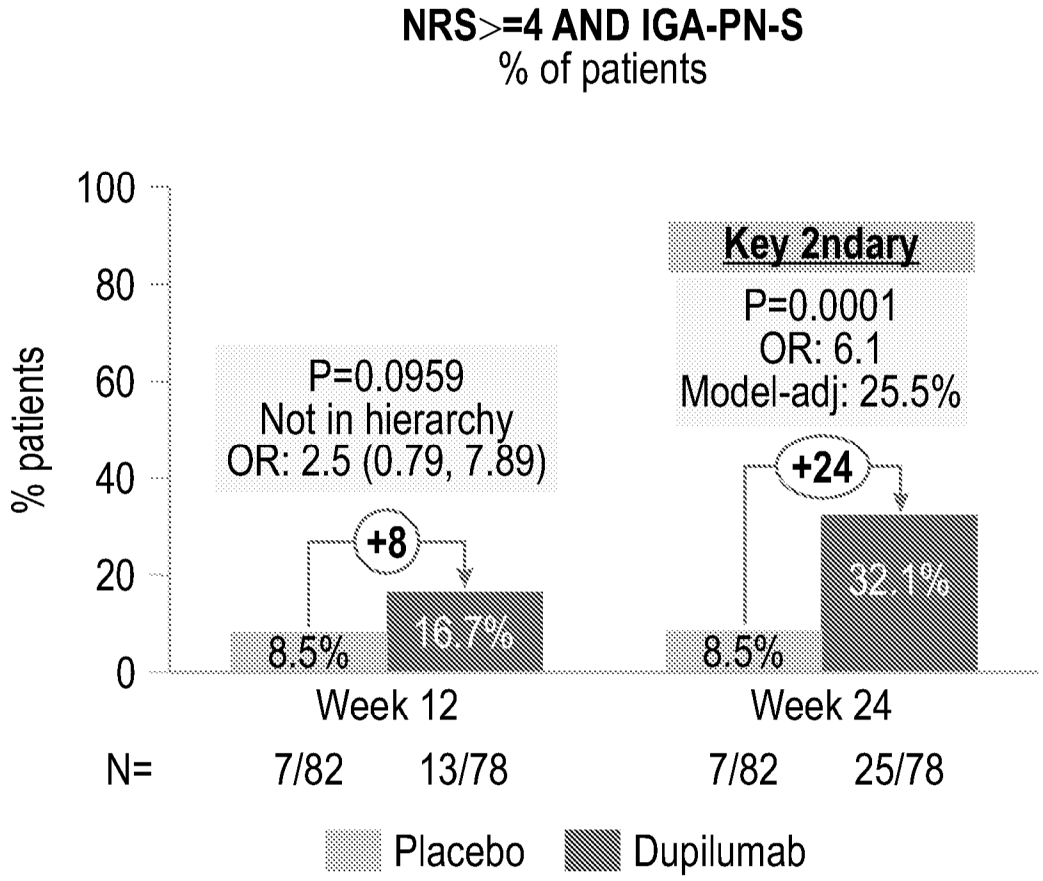

NRS>=4 AND IGA-PN-S
% of patients
% patients
100
80
60
40
20
0
P=0.0959
Not in hierarchy
OR: 2.5 (0.79, 7.89)
+8
8.5%
16.7%
Key 2ndary
P=0.0001
OR: 6.1
Model-adj: 25.5%
+24
8.5%
32.1%
Week 12
Week 24
N=
7/82
13/78
7/82
25/78
Placebo
Dupilumab

FIG. 10B

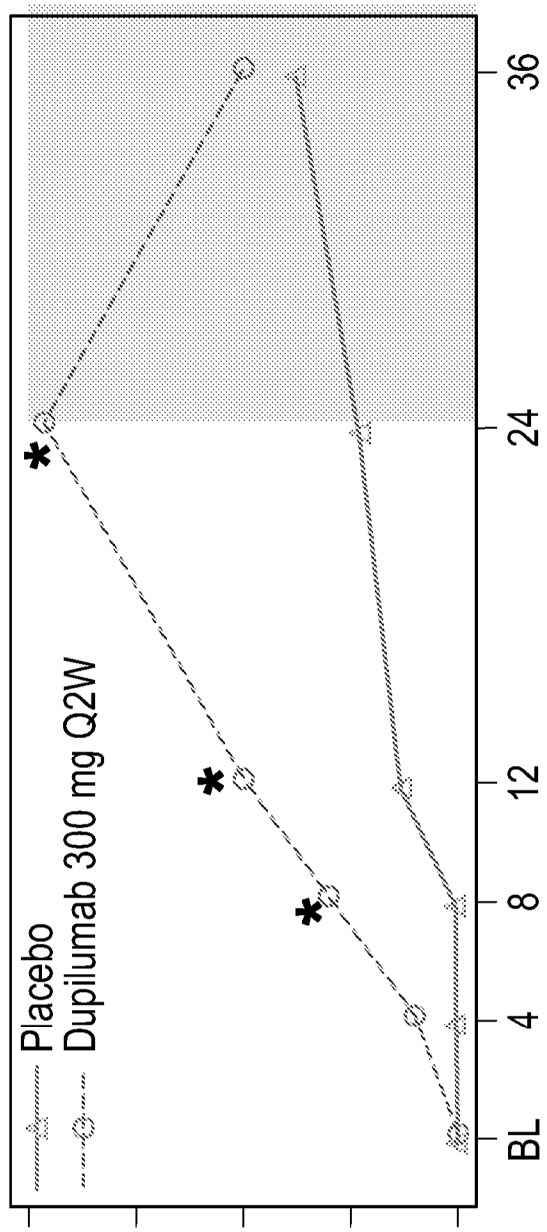

Placebo
Dupilumab 300 mg Q2W
40
30
20
10
0
*
*
*
*
BL
4
8
12
24
36
Week
#Participants
Placebo 76 76 76 76 76 53
mg Q2W 75 75 75 75 75 55

FIG. 10C

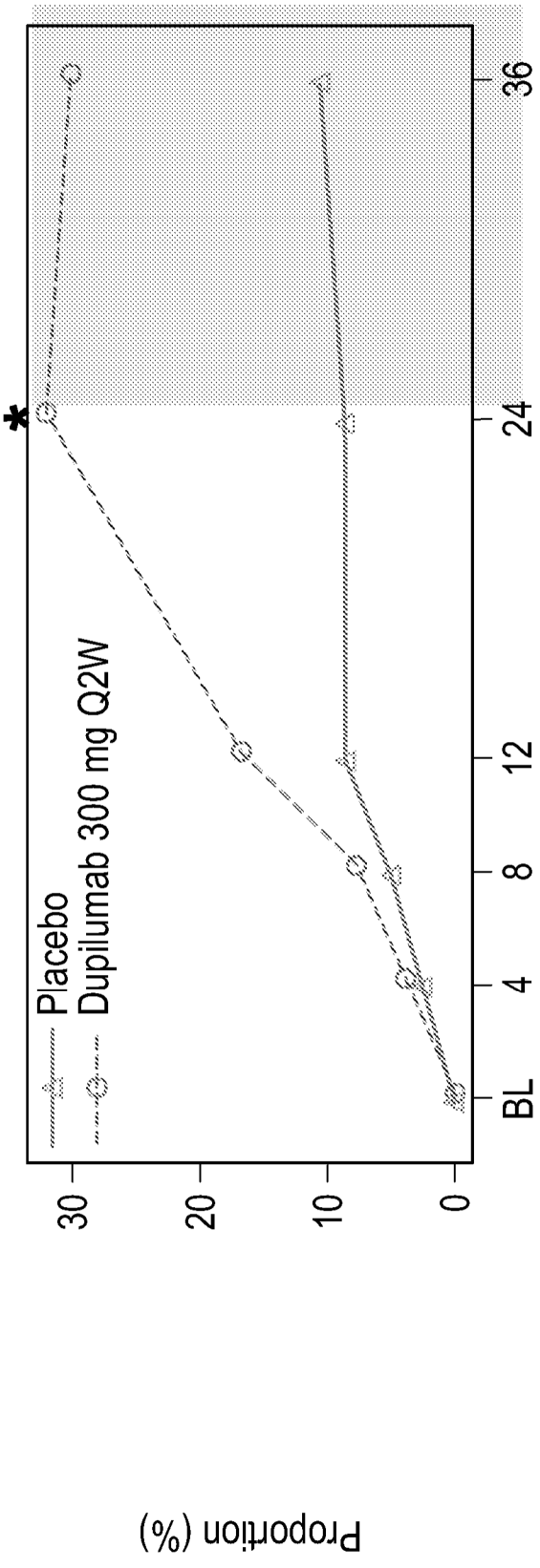

Placebo
Dupilumab 300 mg Q2W
*
30
20
10
0
Proportion (%)
BL
4
8
12
24
36
Week
#Participants
Placebo 82 82 82 82 82 38
Dupilumab 300 mg Q2W 78 78 78 78 78 43

FIG. 10D

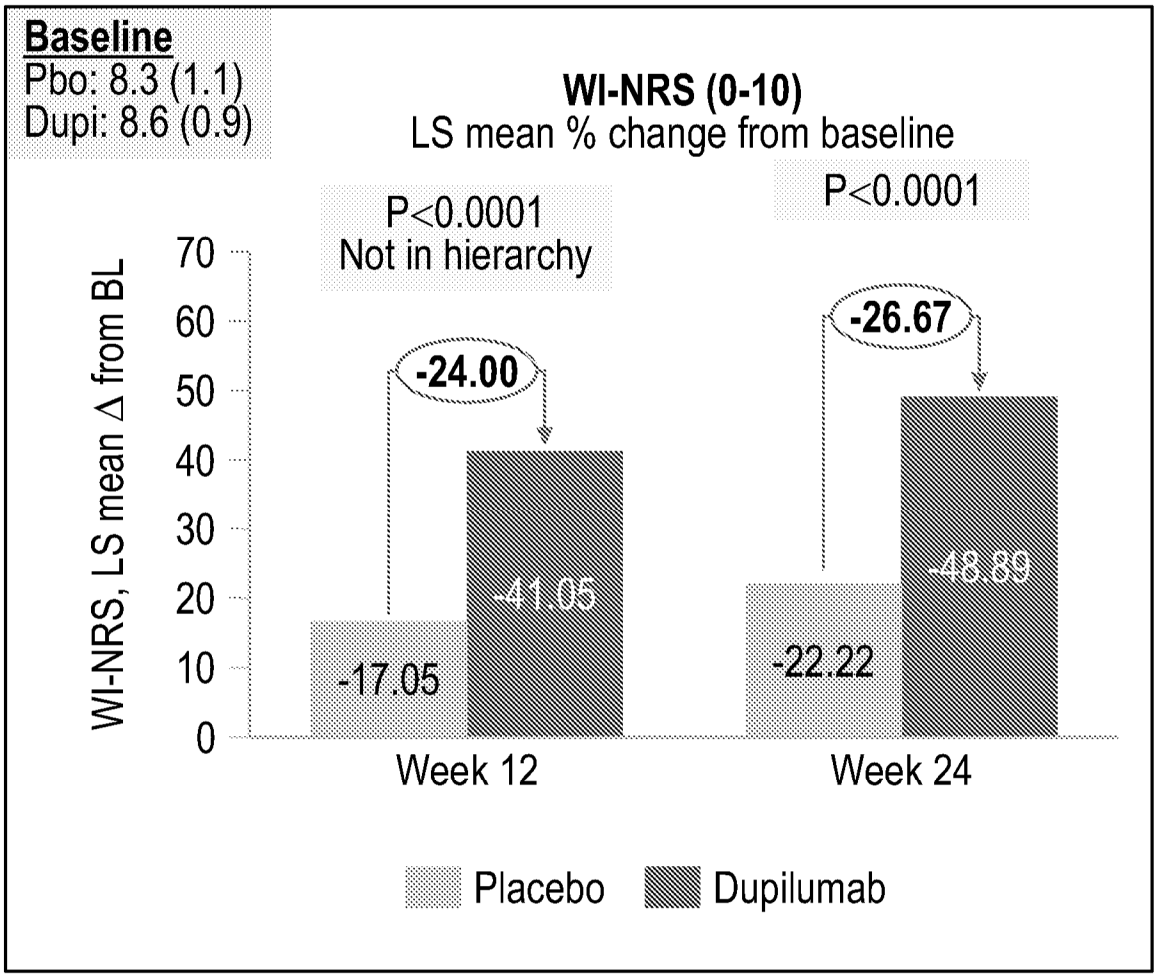

Baseline
Pbo: 8.3 (1.1)
Dupi: 8.6 (0.9)
WI-NRS (0-10)
LS mean % change from baseline
P<0.0001
Not in hierarchy
P<0.0001
-24.00
-26.67
-17.05
-41.05
-22.22
-48.89
WI-NRS, LS mean Δ from BL
70
60
50
40
30
20
10
0
Week 12
Week 24
Placebo
Dupilumab

FIG. 11A

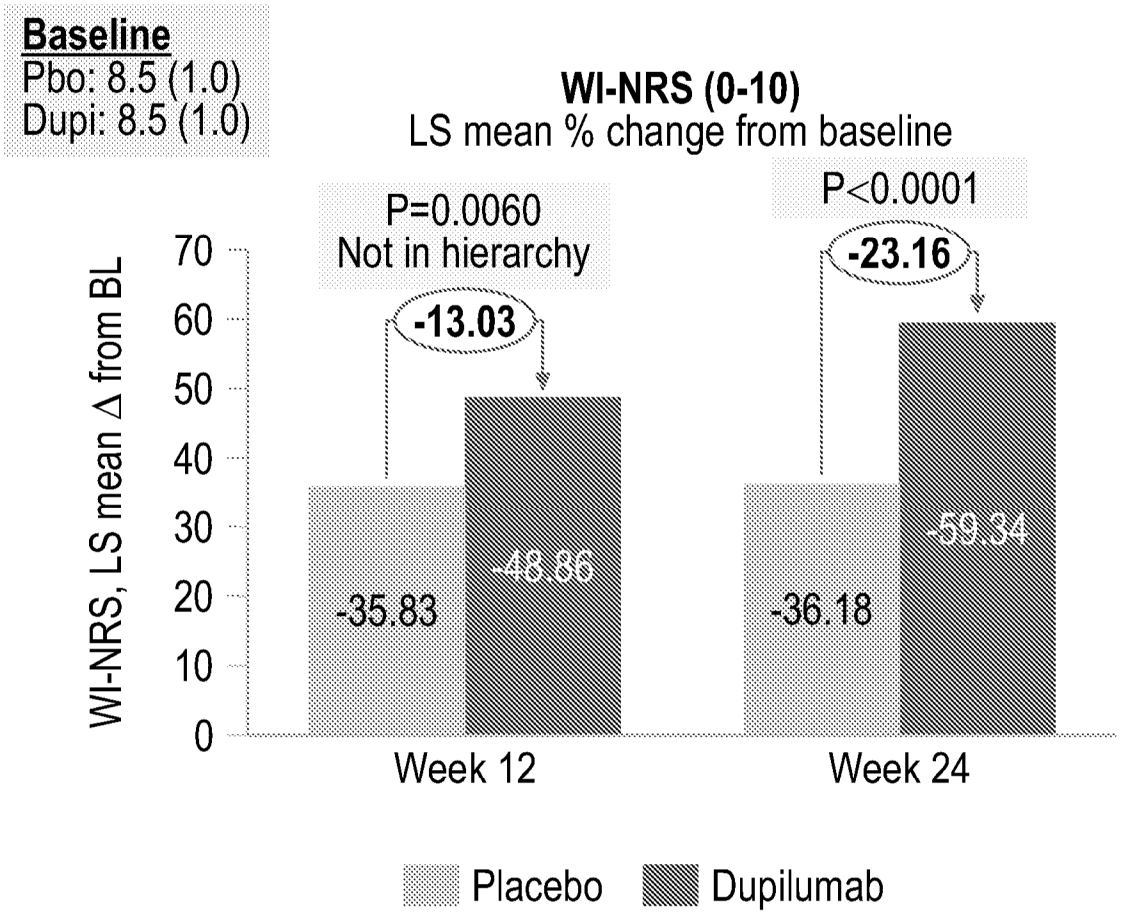
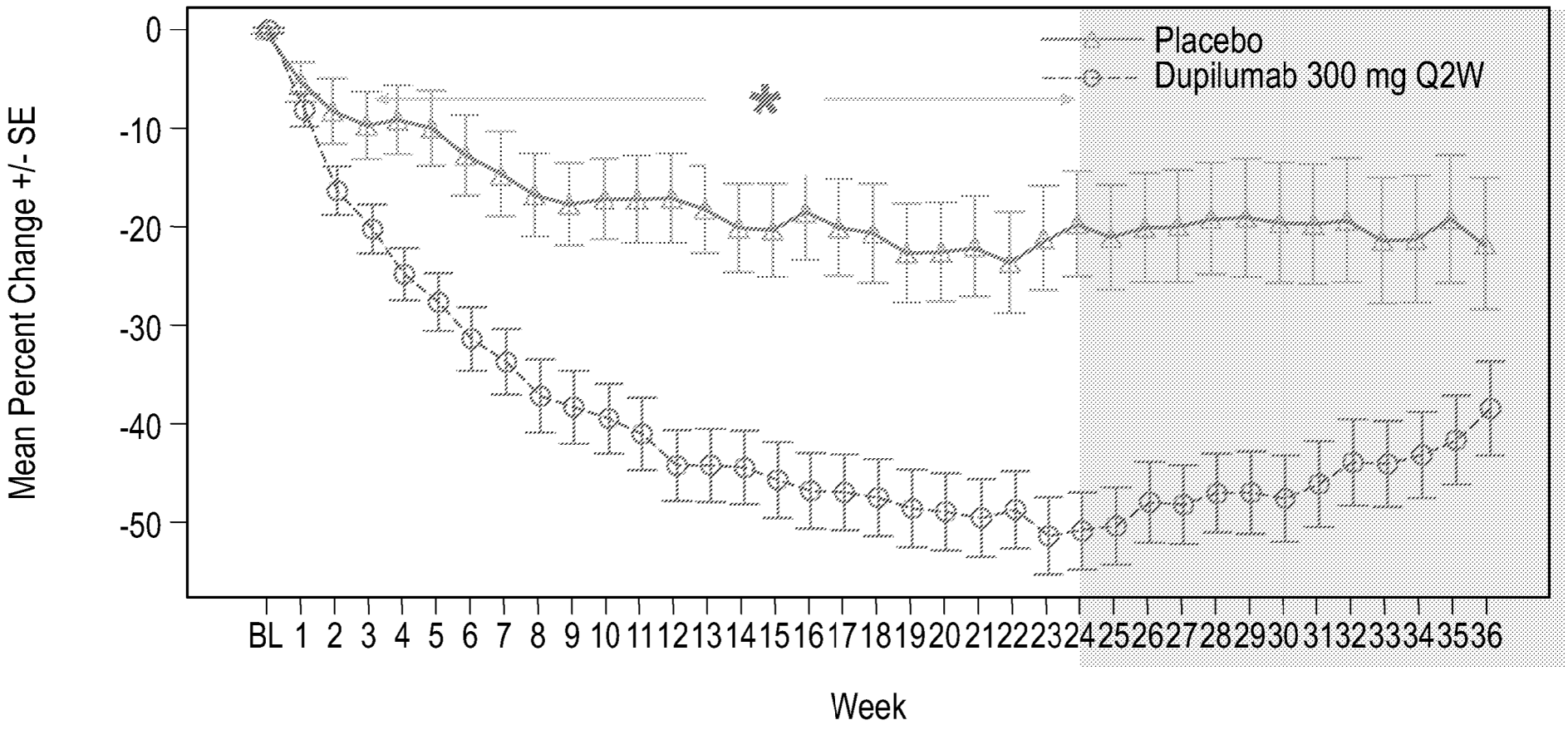

Baseline
Pbo: 8.5 (1.0)
Dupi: 8.5 (1.0)
WI-NRS (0-10)
LS mean % change from baseline
P=0.0060
Not in hierarchy
P<0.0001
-13.03
-23.16
WI-NRS, LS mean Δ from BL
70
60
50
40
30
20
10
0
-35.83
-48.86
-36.18
-59.34
Week 12
Week 24
Placebo
Dupilumab

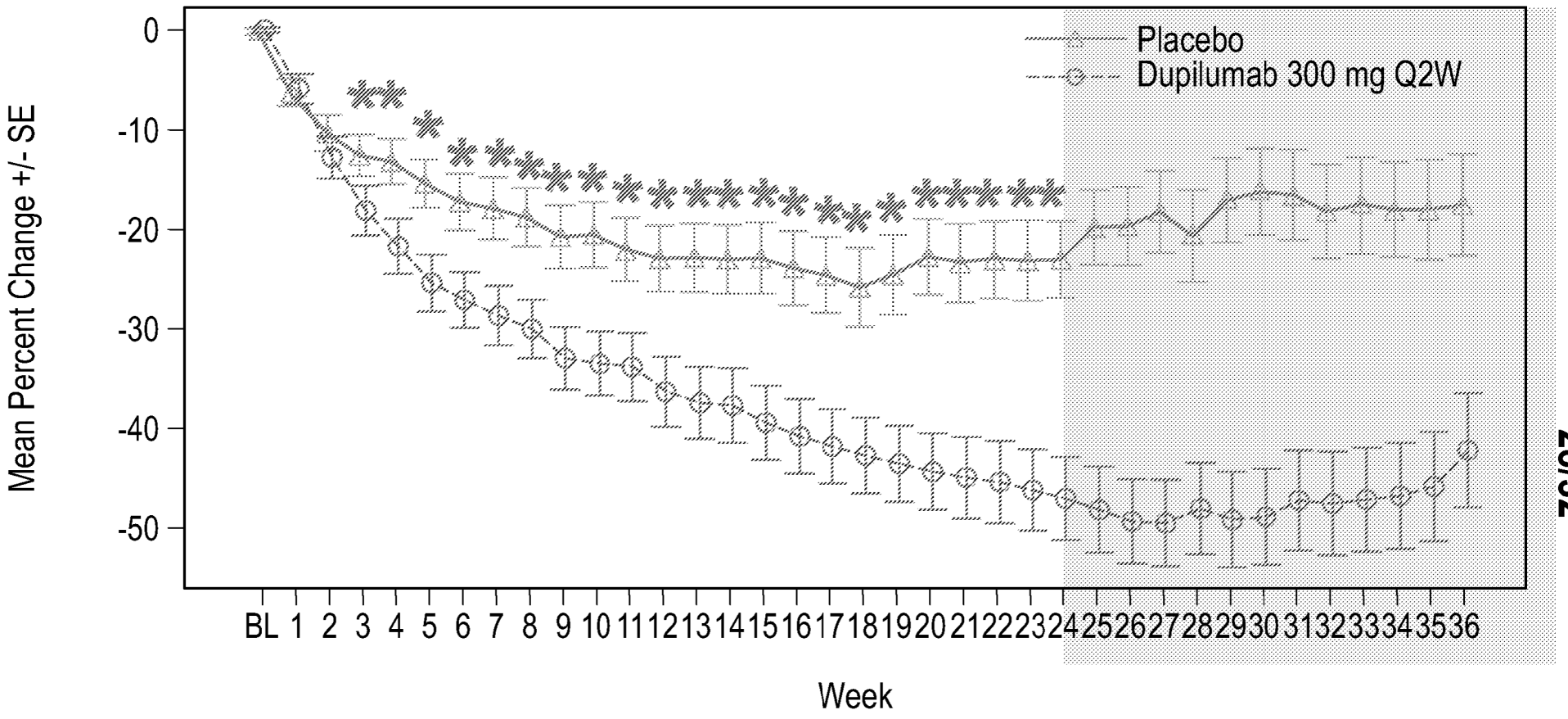
FIG. 11B



#Participants

Placebo	76 76 75 75 75 74 74 73 73 72 72 73 72 73 73 72 71 71 71 70 69 68 68 68 66 57 64 61 61 58 59 59 57 57 55 53 54
Dupilumab 300 mg Q2W	75 75 75 75 75 74 75 75 75 75 75 75 75 75 75 75 75 75 74 75 75 75 75 75 72 70 70 69 69 69 68 67 65 64 60 56

FIG. 11C



#Participants

Placebo	82 82 81 81 81 81 80 78 79 79 78 79 79 79 79 79 77 77 77 76 74 74 74 73 74 70 70 62 60 58 53 51 48 45 44 41 39
Dupilumab 300 mg Q2W	78 78 77 77 77 77 77 76 77 77 76 77 77 77 77 77 77 77 77 77 77 76 76 75 76 70 68 66 61 58 57 54 51 51 50 49 46

FIG. 11D

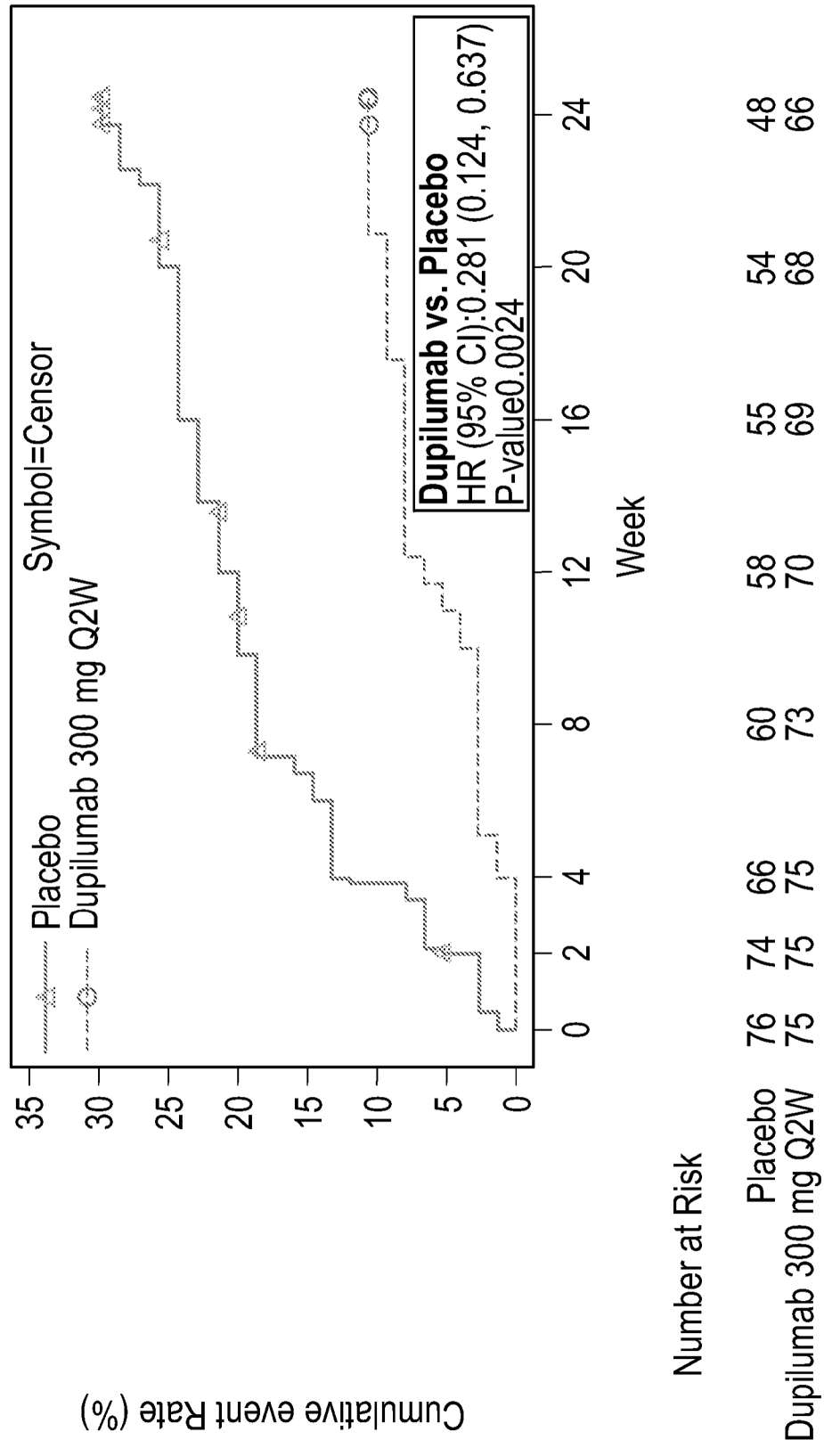

Placebo
Dupilumab 300 mg Q2W
Symbol=Censor
Dupilumab vs. Placebo
HR (95% CI):0.281 (0.124, 0.637)
P-value0.0024
Cumulative event Rate (%)
0
5
10
15
20
25
30
35
Week
0
2
4
8
12
16
20
24
Number at Risk
Placebo 76 74 66 60 58 55 54 48
Dupilumab 300 mg Q2W 75 75 75 73 70 69 68 66

FIG. 12A

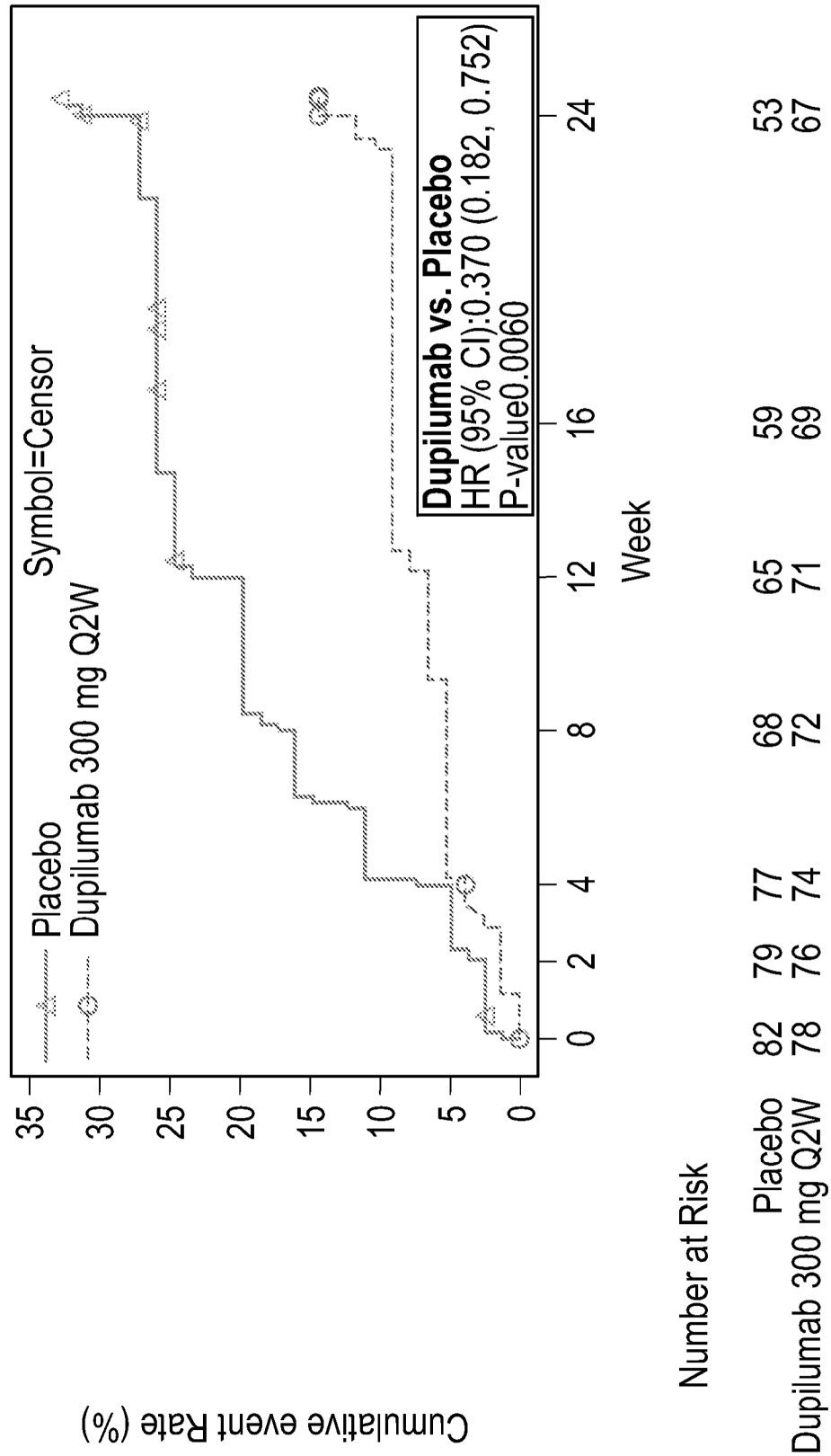

Placebo
Dupilumab 300 mg Q2W
Symbol=Censor
Dupilumab vs. Placebo
HR (95% CI):0.370 (0.182, 0.752)
P-value0.0060
Cumulative event Rate (%)
0
5
10
15
20
25
30
35
Week
0
2
4
8
12
16
24
Number at Risk
Placebo 82 79 77 68 65 59 53
Dupilumab 300 mg Q2W 78 76 74 72 71 69 67

FIG. 12B

Baseline
IGA PN-S 4
Avg WI-NRS 9.4

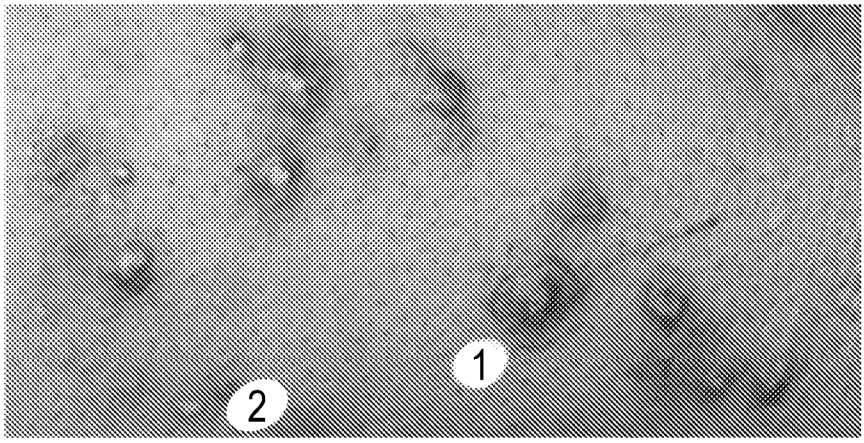
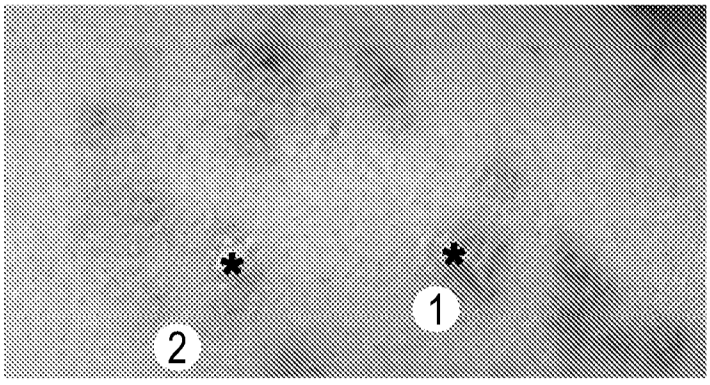


FIG. 13A

Week 24
IGA PN-S 0
Avg WI-NRS 1.3



* Biopsy scars from sub-study

FIG. 13B

Baseline Disease characteristics

	PRIME2/EFC16460			PRIME/EFC16459		
	Pbo n=82	Dupilumab 300 mg q2w n=78	Overall n=160	Pbo n=76	Dupilumab 300 mg q2w n=75	Overall n=151
n (ITT)	82	78	160	76	75	151
Duration of PN (yr), mean (SD)	5.48 (6.97)	5.36 (6.90)	5.42 (6.92)	5.40 (6.21)	6.01 (7.55)	5.70 (6.89)
History of atopy, n(%)	40 (48.8%)	34 (43.6%)	74 (46.3%)	28 (36.8%)	33 (44.0%)	61 (40.4%)
Stable use of TCS/TCI, n(%)	46 (56.1%)	44 (56.4%)	90 (56.3%)	45 (59.2%)	47 (62.7%)	92 (60.9%)
WI-NRS (0-10) , mean (SD)	8.5 (1.0)	8.5 (1.0)	8.5 (1.0)	8.3 (1.1)	8.6 (0.9)	8.5 (1.0)
IGA PN-S (0-4), n (%)						
3	49 (60.5%)	49 (62.8%)	98 (61.6%)	53 (70.7%)	54 (72.0%)	107 (71.3%)
4	32 (39.5%)	29 (37.2%)	61 (38.4%)	22 (29.3%)	21 (28.0%)	43 (28.7%)
IGA PN-A (0-4), n (%)						
3	42 (51.9%)	44 (56.4%)	86 (54.1%)	41 (54.7%)	43 (57.3%)	84 (56.0%)
4	35 (43.2%)	31 (39.7%)	66 (41.5%)	30 (40.0%)	29 (38.7%)	59 (39.3%)
Skin-Pain NRS (0-10), mean (SD)	7.1 (2.5)	7.3 (2.54)	7.2 (2.4)	7.2 (2.3)	7.2 (2.5)	7.2 (2.4)
Sleep NRS (0-10), mean (SD)	4.2 (2.5)	4.4 (2.3)	4.3 (2.4)	4.3 (2.2)	4.4 (2.4)	4.3 (2.3)
DLQI (0-30), mean (SD)	18.2 (7.0)	18.2 (6.5)	18.2 (6.7)	15.7 (7.3)	17.8 (7.1)	16.7 (7.2)
HADS [0-42], mean(SD)	15.9 (8.4)	16.2 (7.7)	16.0 (8.0)	14.3 (8.0)	14.5 (8.2)	14.4 (8.1)
Baseline exact number of lesions in representative area, mean(SD)	26.4 (18.8)	25.5 (18.7)	26.0 (18.7)	25.1 (16.7)	27.0 (26.7)	26.1 (22.2)

FIG. 14