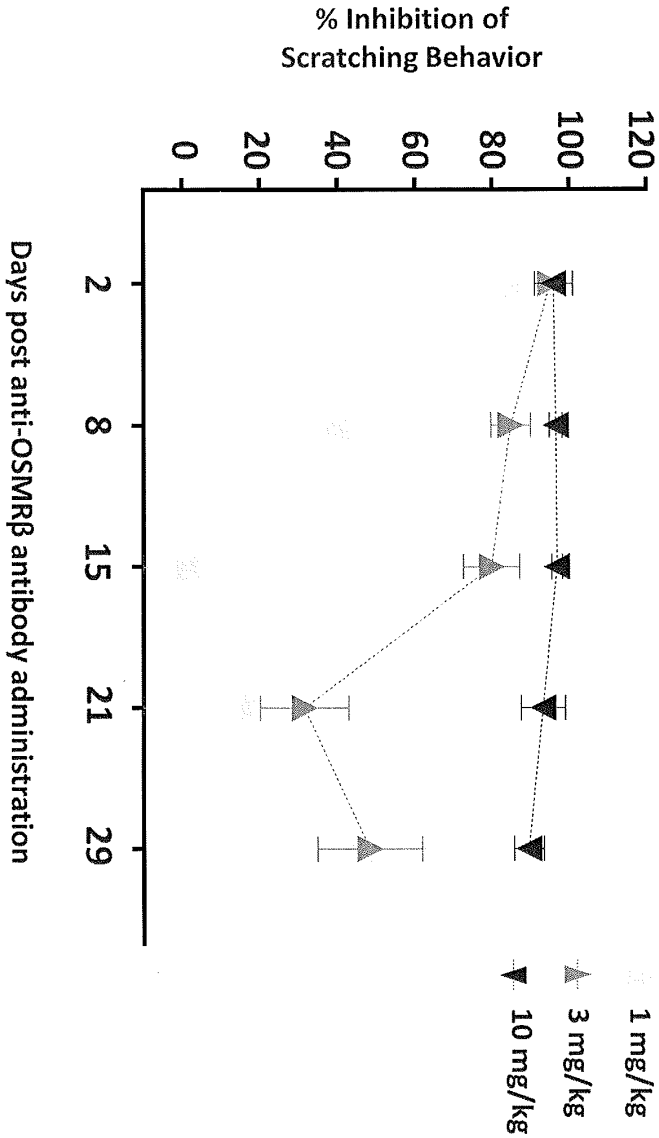
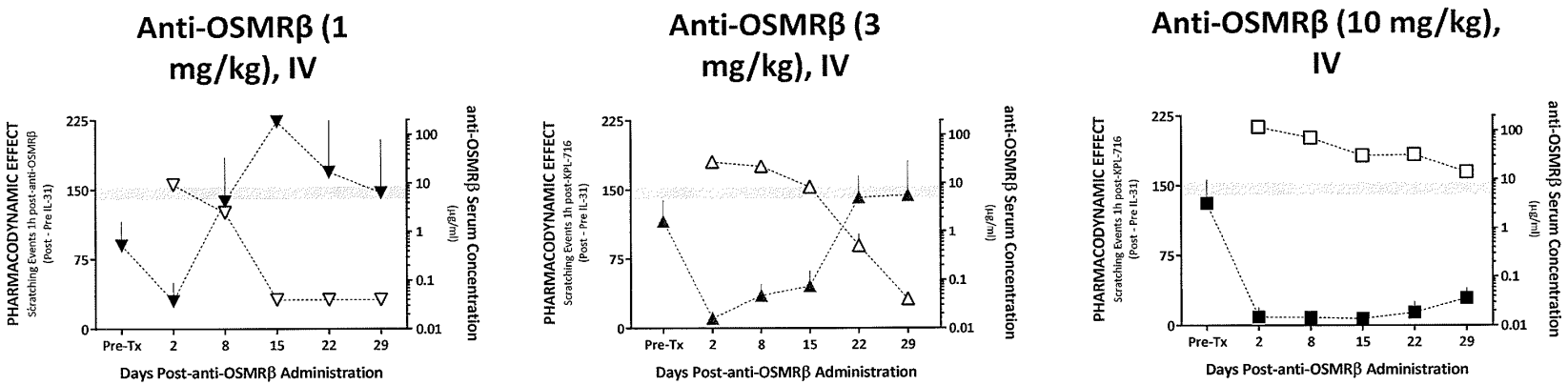

% Inhibition of
Scratching Behavior
0
20
40
60
80
100
120
2
8
15
21
29
Days post anti-OSMRβ antibody administration
1 mg/kg
3 mg/kg
10 mg/kg

FIGURE 1A



Efficacious Concentration Range defined via PK/PD correlation = 5 – 8.5 µg/mL

Anti-OSMRβ was administered on day 1 via IV route

Filled symbols represent Pharmacodynamic Effect on the left vertical axis

Open symbols represent Pharmacokinetic Effect on the right vertical axis

Scratching events are calculated as post–IL-31 challenge events minus pre–IL-31 challenge events.
N=6 animals were treated per dose group
Lower limit of quantification = 0.04 µg/mL.

FIGURE 1B

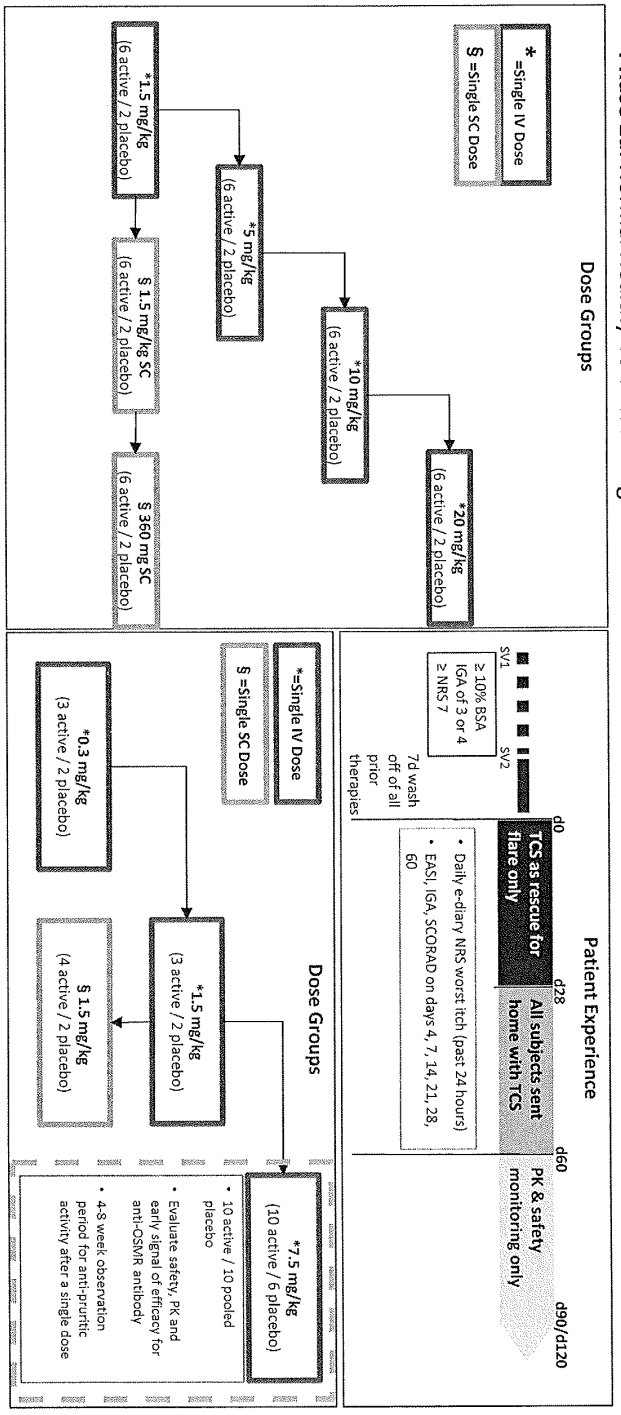

Phase 1a: Normal Healthy Volunteer Single Dose
Dose Groups
* =Single IV Dose
§ =Single SC Dose
*1.5 mg/kg
(6 active / 2 placebo)
*5 mg/kg
(6 active / 2 placebo)
*10 mg/kg
(6 active / 2 placebo)
*20 mg/kg
(6 active / 2 placebo)
§ 1.5 mg/kg SC
(6 active / 2 placebo)
§ 360 mg SC
(6 active / 2 placebo)
Phase 1b: Subjects with Atopic Dermatitis
Patient Experience
SV1
SV2
≥ 10% BSA
IGA of 3 or 4
≥ NRS 7
7d wash off of all prior therapies
d0
TCS as rescue for flare only
d28
All subjects sent home with TCS
d60
PK & safety monitoring only
d90/d120
• Daily e-diary NRS worst itch (past 24 hours)
• EASI, IGA, SCORAD on days 4, 7, 14, 21, 28, 60
Dose Groups
*=Single IV Dose
§ =Single SC Dose
*0.3 mg/kg
(3 active / 2 placebo)
*1.5 mg/kg
(3 active / 2 placebo)
§ 1.5 mg/kg
(4 active / 2 placebo)
*7.5 mg/kg
(10 active / 6 placebo)
• 10 active / 10 pooled placebo
• Evaluate safety, PK and early signal of efficacy for anti-OSMR antibody
• 4-8 week observation period for anti-pruritic activity after a single dose

FIGURE 2

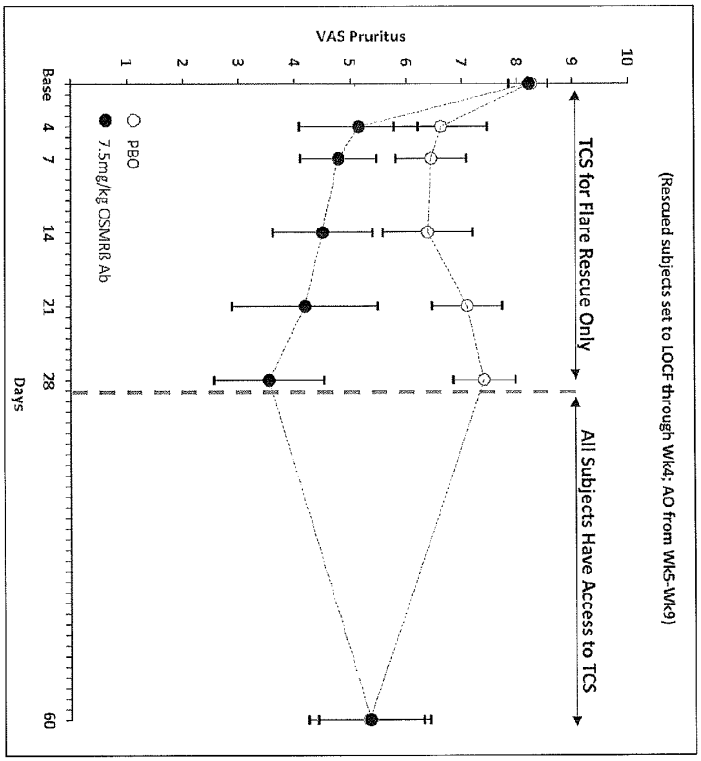


FIGURE 3A

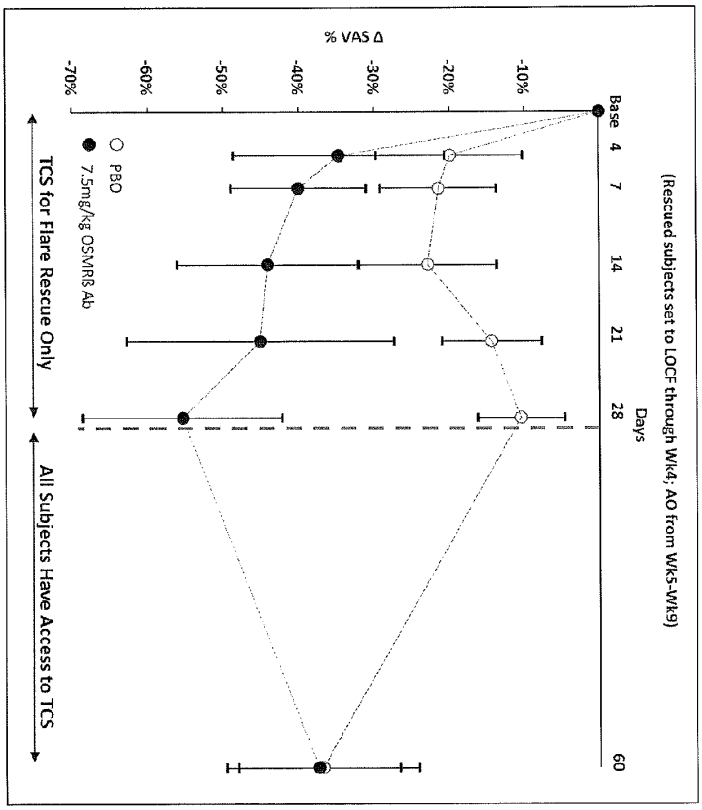


FIGURE 3B

LOCF = Last Observed Carried Forward
AO = as observed

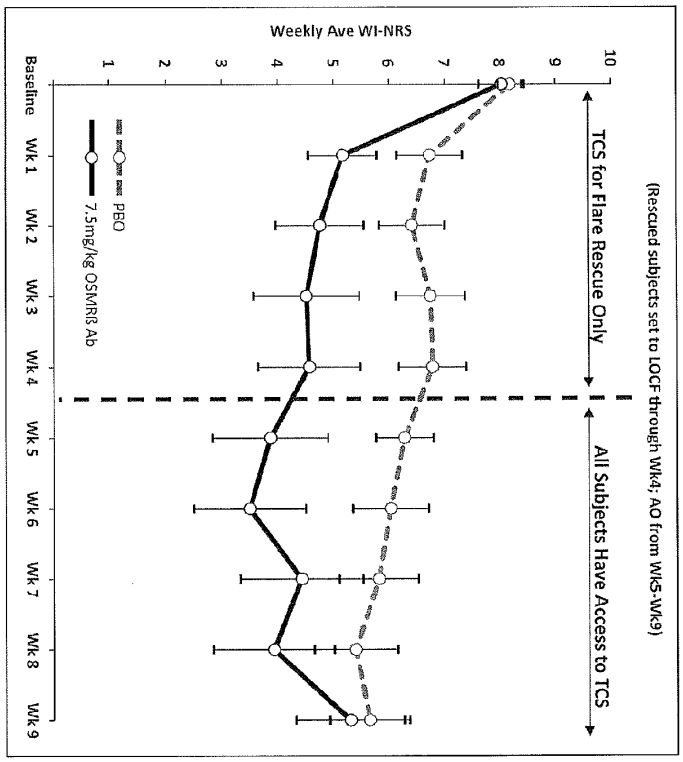


FIGURE 3C

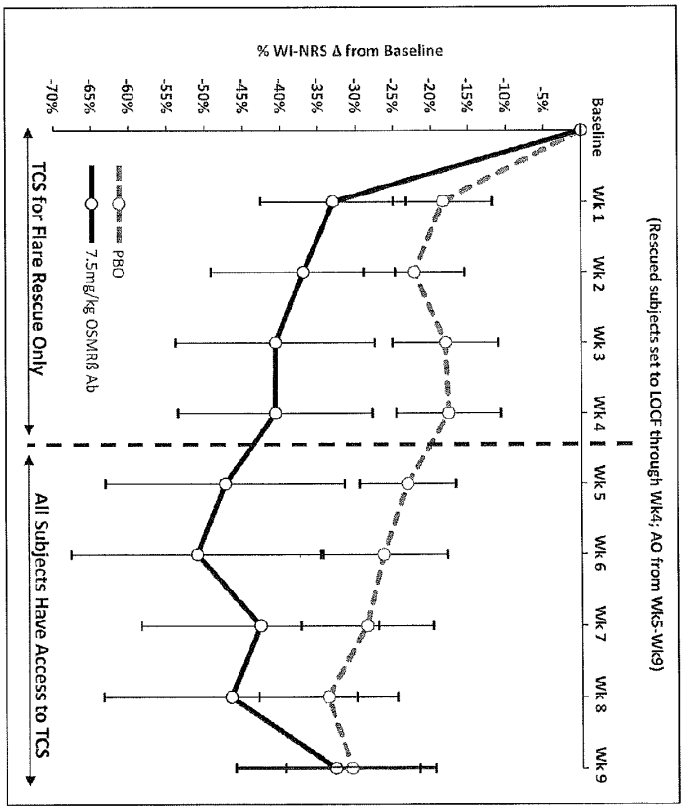


FIGURE 3D

LOCF = Last Observed Carried Forward
AO = as observed

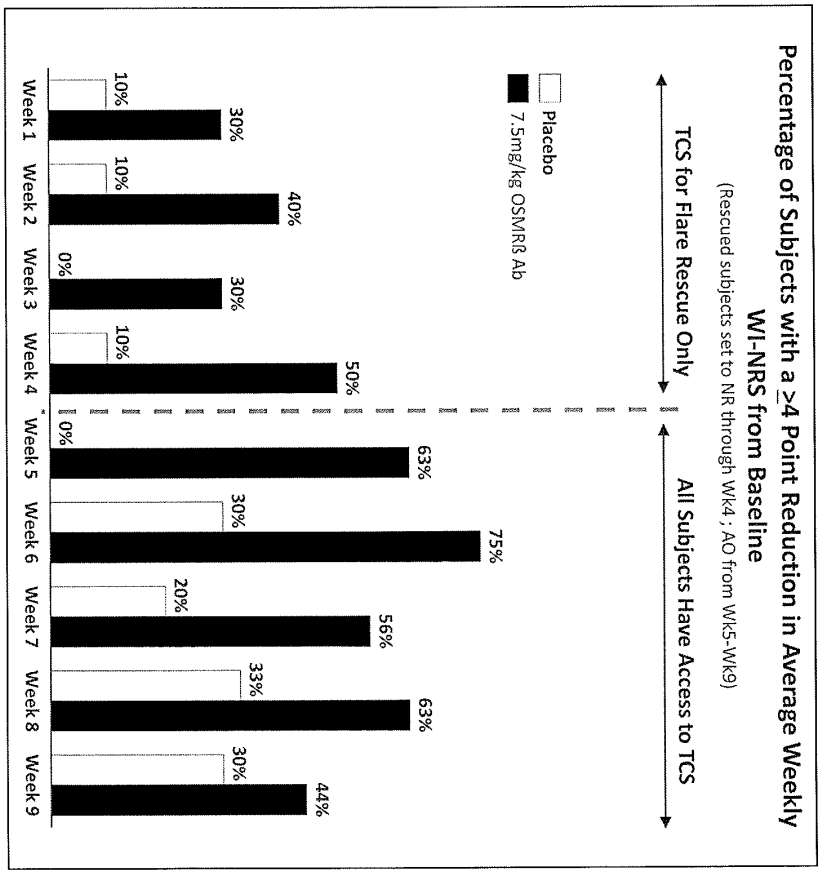

Percentage of Subjects with a ≥4 Point Reduction in Average Weekly WI-NRS from Baseline
(Rescued subjects set to NR through Wk4 ; AO from Wk5-Wk9)
TCS for Flare Rescue Only
All Subjects Have Access to TCS
Placebo
7.5mg/kg OSMRß Ab
Week 1 10% 30%
Week 2 10% 40%
Week 3 0% 30%
Week 4 10% 50%
Week 5 0% 63%
Week 6 30% 75%
Week 7 20% 56%
Week 8 33% 63%
Week 9 30% 44%
NR = non-responder
AO = as observed

FIGURE 4

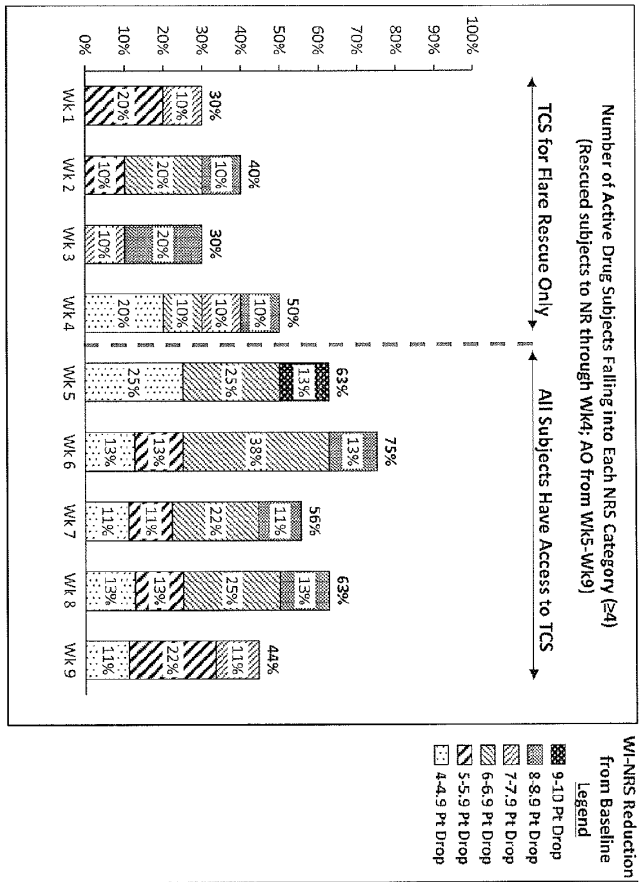


FIGURE 5A

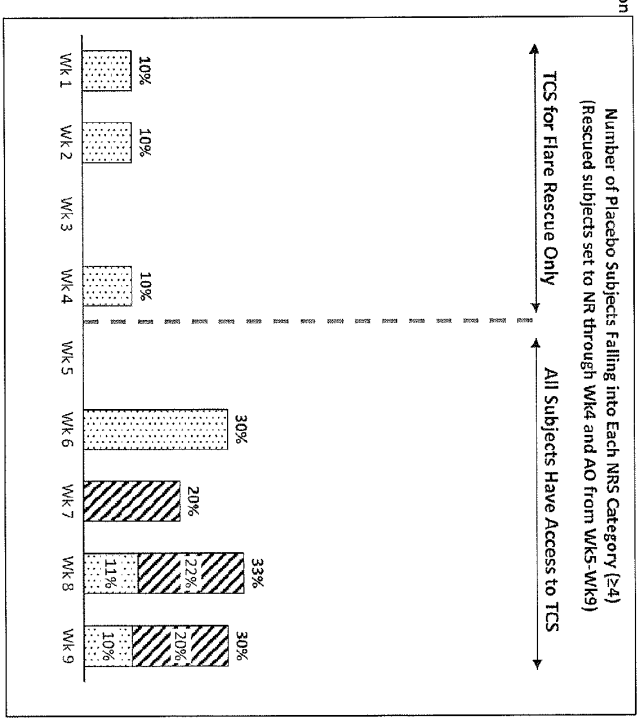


FIGURE 5B

NR = non-responder
AO = as observed

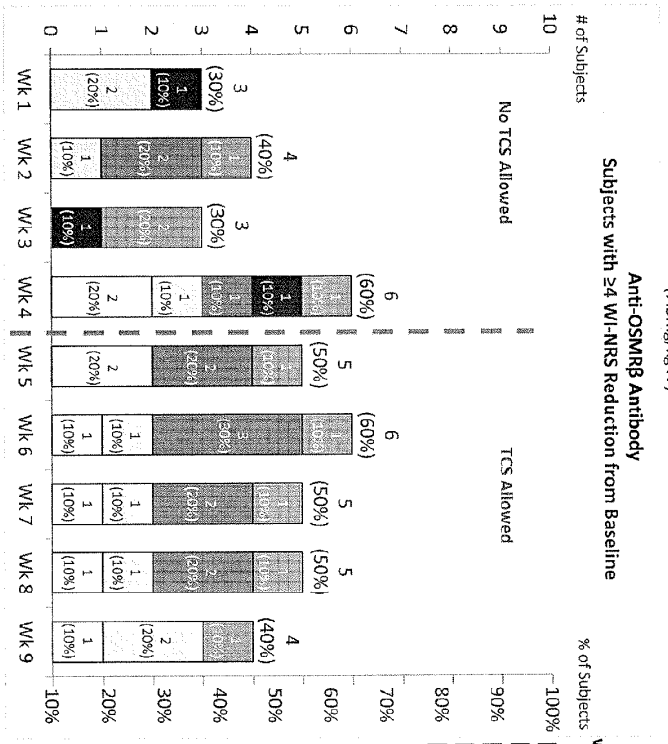


FIGURE 5C

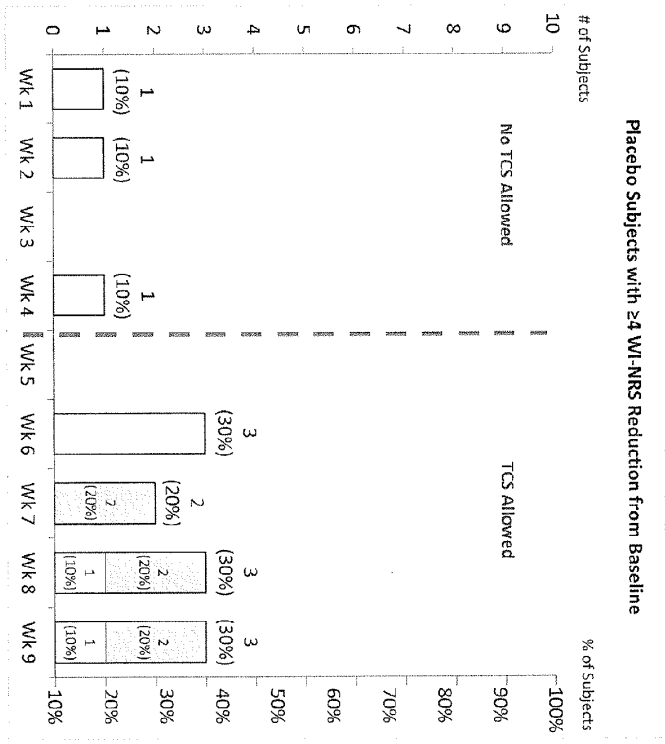


FIGURE 5D

WI-NRS = Worst Itch Numerical Rating Scale

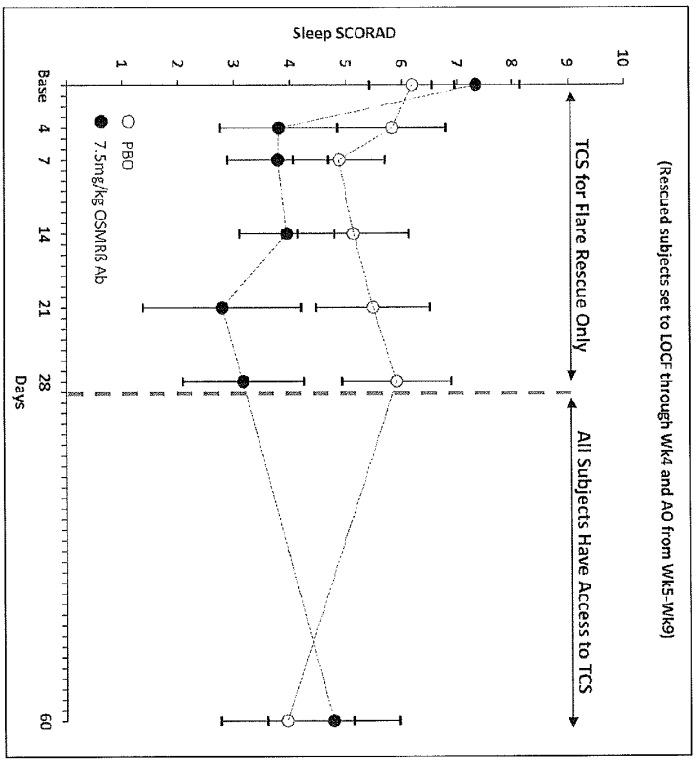


FIGURE 6A

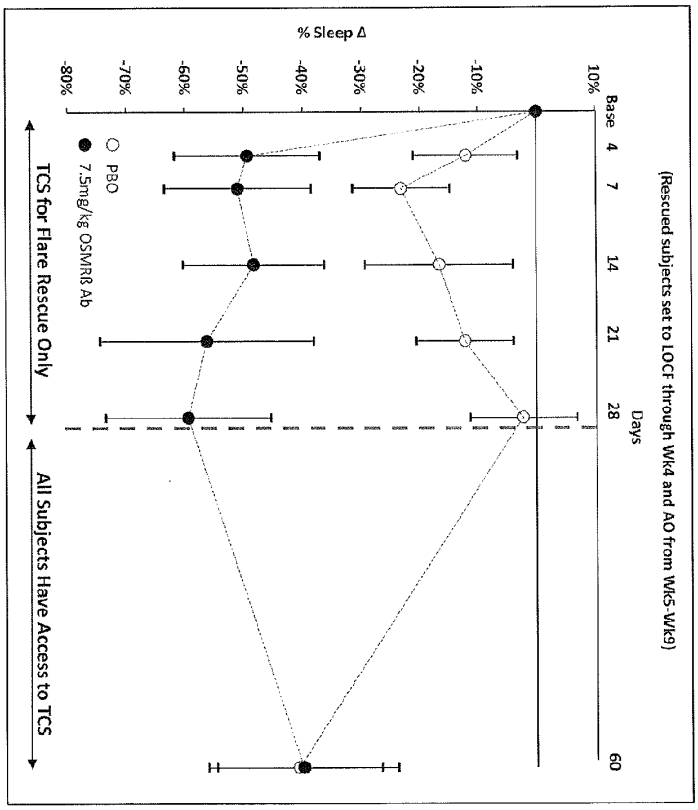


FIGURE 6B

LOCF = Last Observed Carried Forward
AO = as observed

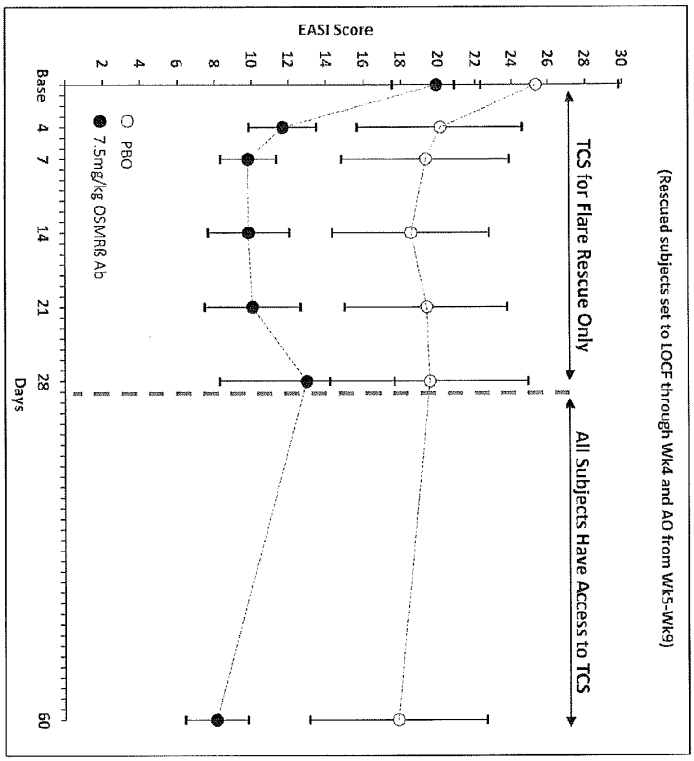


FIGURE 7A

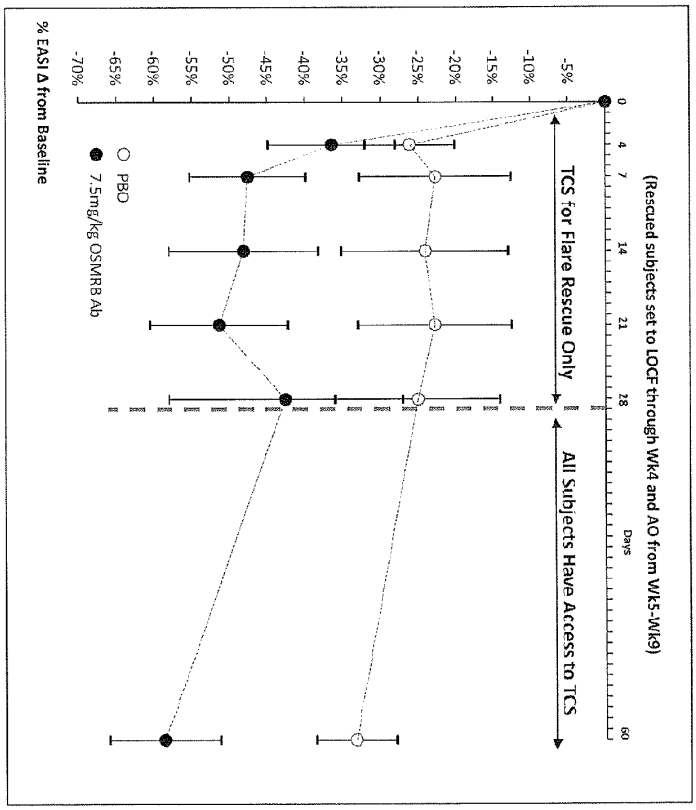


FIGURE 7B

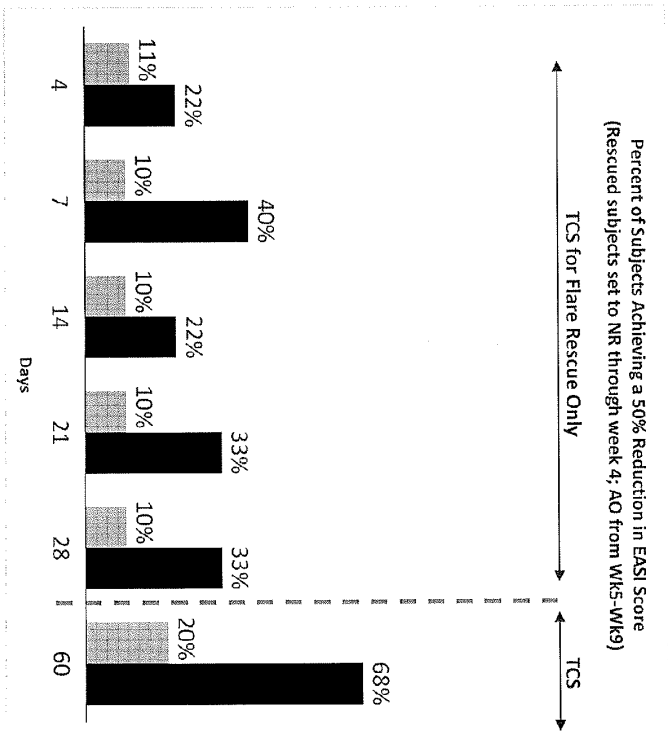


FIGURE 8A

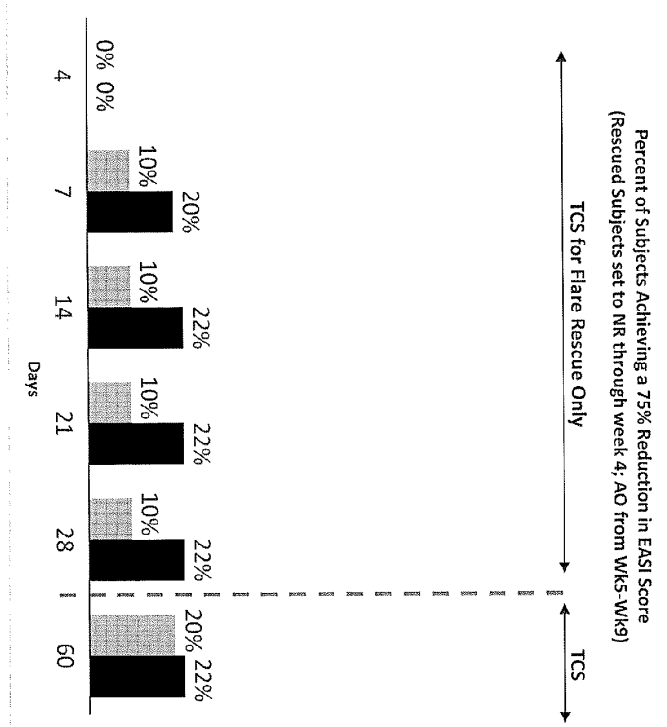


FIGURE 8B

NR = non-responder
AO = as observed

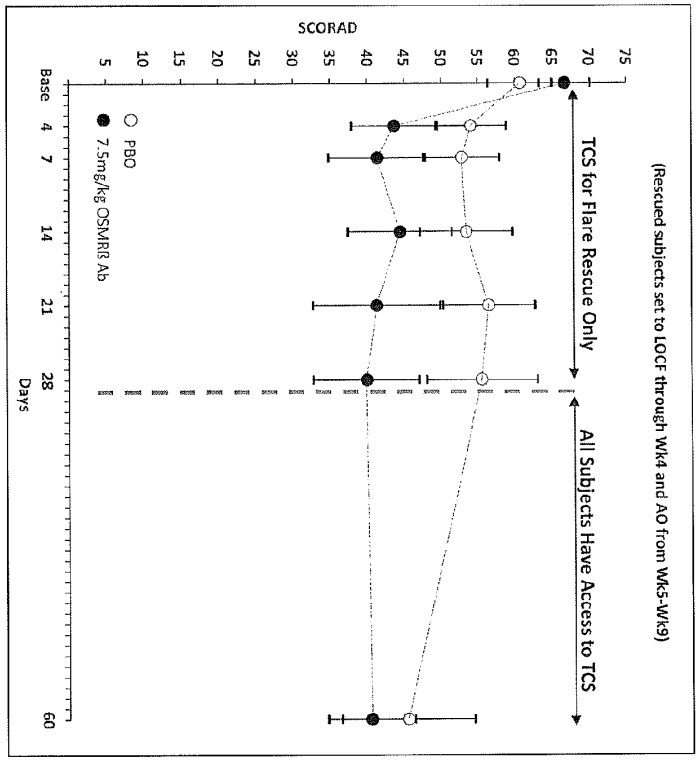


FIGURE 9A

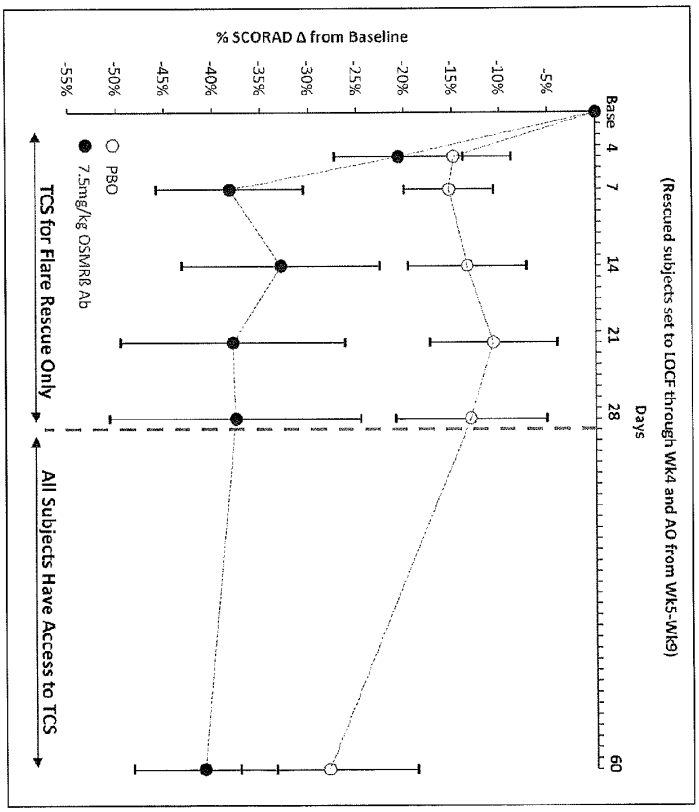


FIGURE 9B

LOCF = Last Observed Carried Forward
AO = as observed

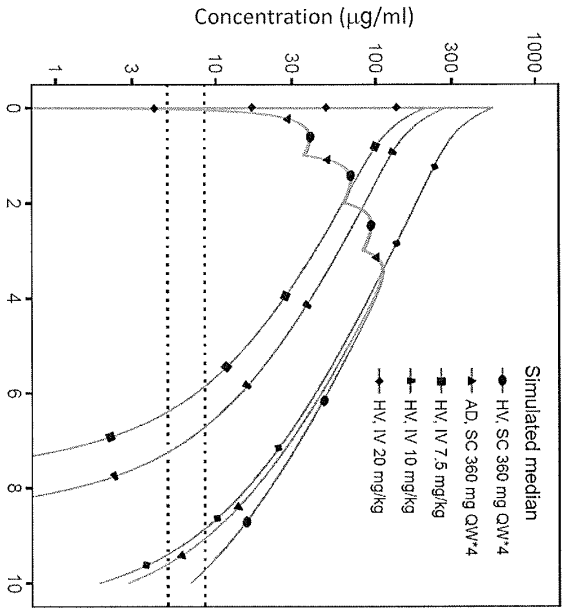


FIGURE 10A

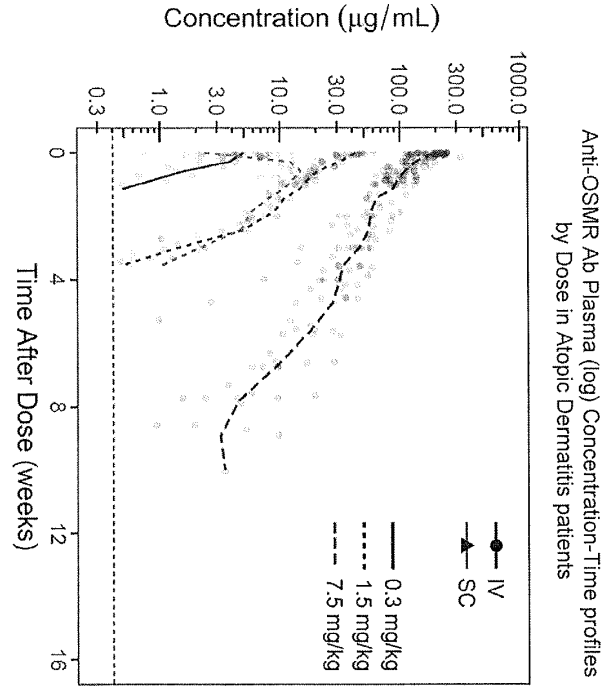


FIGURE 10B

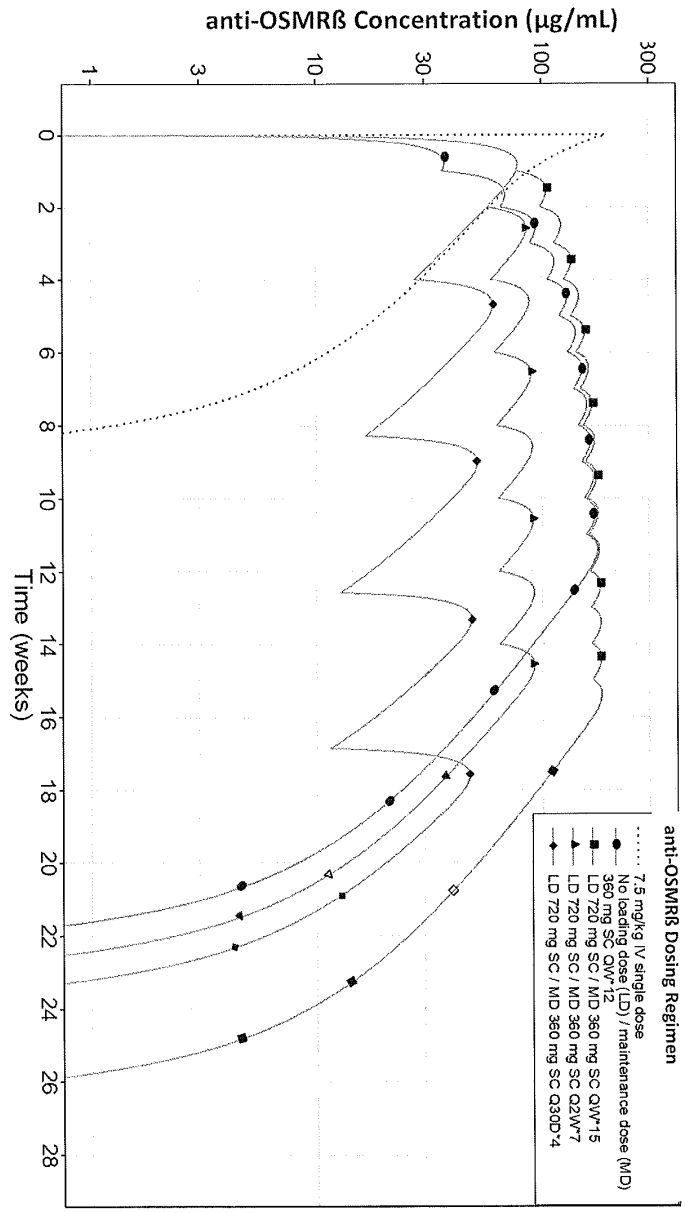

anti-OSMRß Concentration (µg/mL)
300
100
30
10
3
1
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Time (weeks)
anti-OSMRß Dosing Regimen
7.5 mg/kg IV single dose
No loading dose (LD) / maintenance dose (MD)
360 mg SC QW*12
LD 720 mg SC / MD 360 mg SC QW*15
LD 720 mg SC / MD 360 mg SC Q2W*7
LD 720 mg SC / MD 360 mg SC Q30D*4

FIGURE 10C

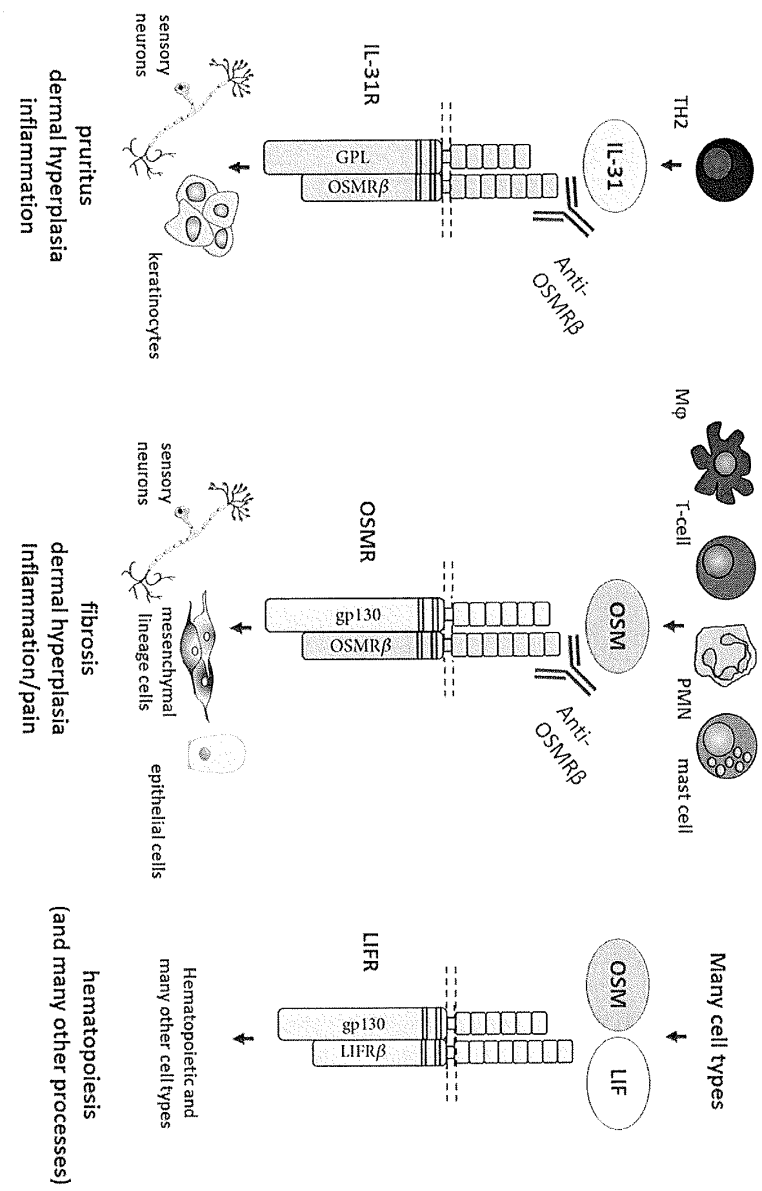
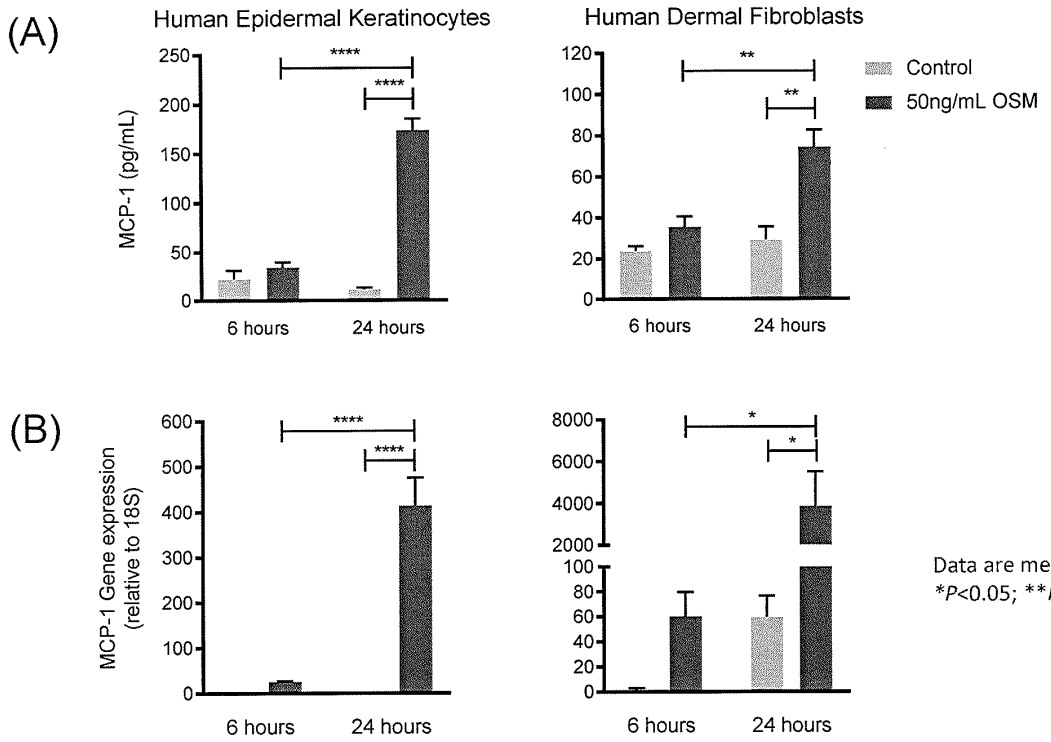

TH2
IL-31
IL-31R
GPL
OSMRβ
Anti-OSMRβ
sensory neurons
keratinocytes
pruritus
dermal hyperplasia
inflammation
Mφ
T-cell
PMN
mast cell
OSM
OSMR
gp130
OSMRβ
Anti-OSMRβ
sensory neurons
mesenchymal lineage cells
epithelial cells
fibrosis
dermal hyperplasia
Inflammation/pain
Many cell types
OSM
LIF
LIFR
gp130
LIFRβ
Hematopoietic and many other cell types
hematopoiesis
(and many other processes)

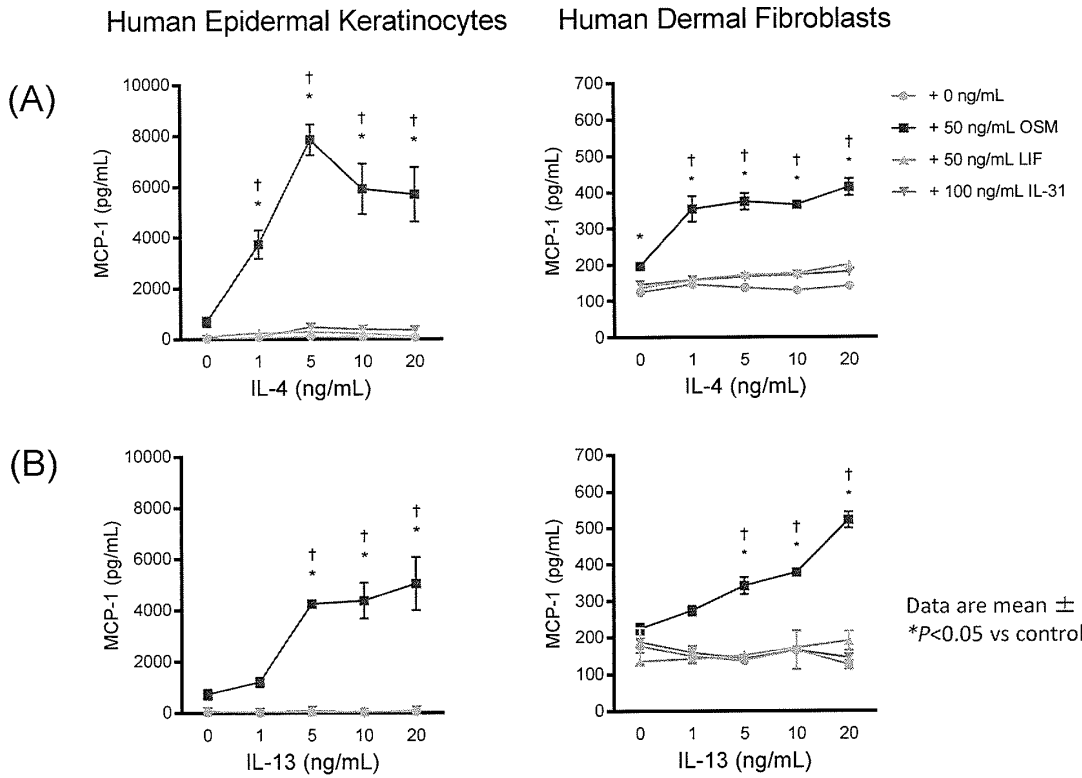
FIGURE 11



Data are mean ± SEM; two-way ANOVA; *P<0.05; **P<0.01; ****P<0.0001.

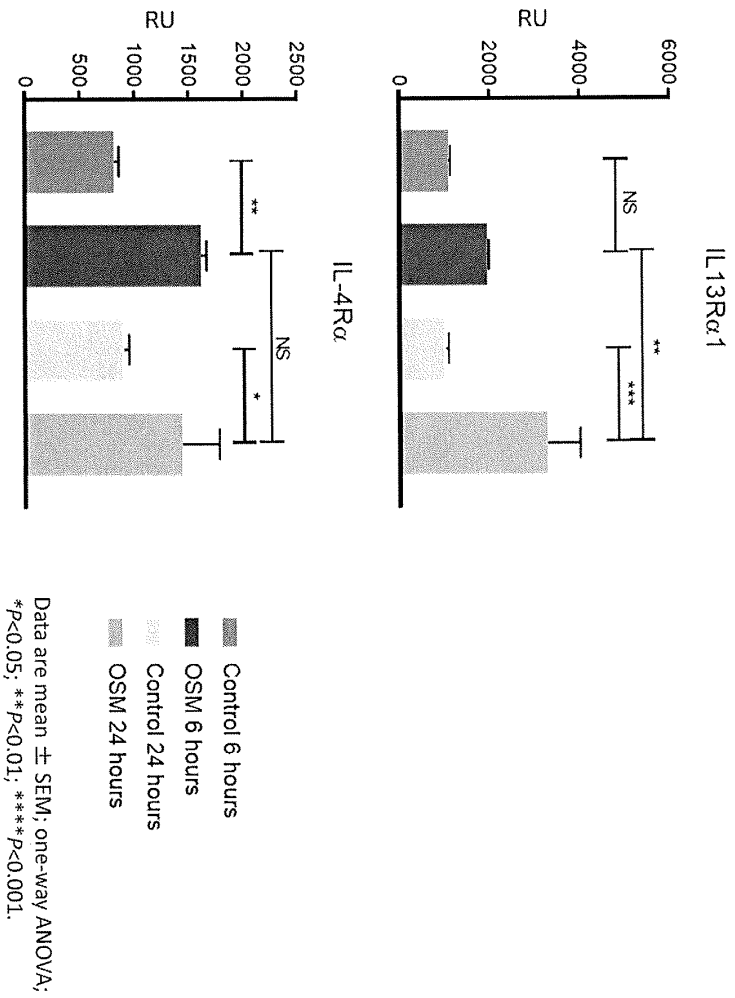
HDF = human dermal fibroblasts; HEK = human epidermal keratinocytes; MCP-1 = monocyte chemoattractant protein-1; OSM = oncostatin M; RNA = ribonucleic acid; qRT-PCR = real-time quantitative reverse transcription polymerase chain reaction.

FIGURE 12



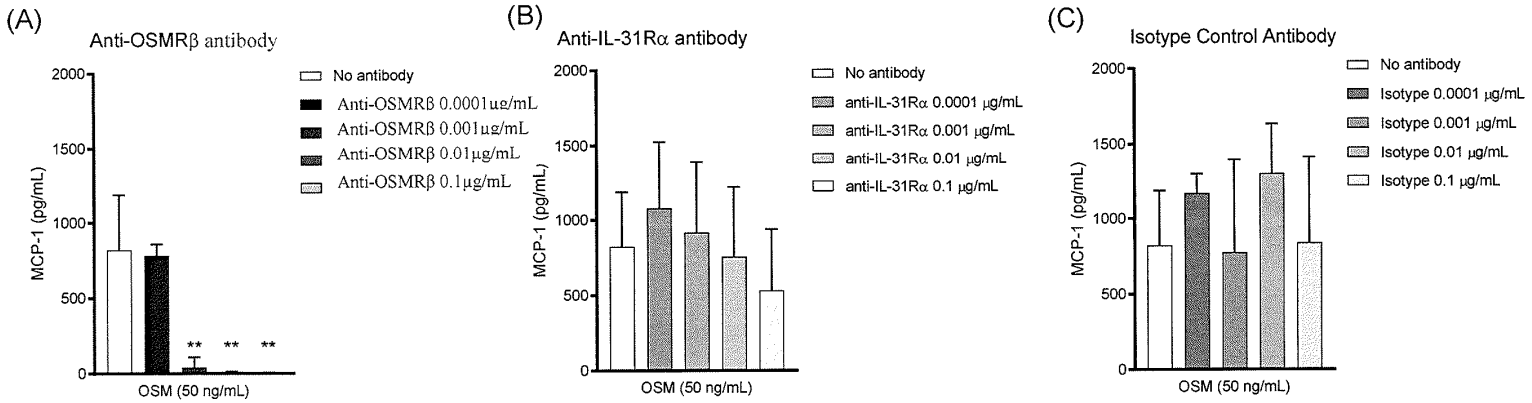
HDF = human dermal fibroblasts, HEK = human epidermal keratinocytes, IL = interleukin, LIF = leukemia inhibitory factor, MCP-1 = monocyte chemoattractant protein-1 OSM = oncostatin M.

FIGURE 13



Data are mean ± SEM; one-way ANOVA; *$P<0.05$; **$P<0.01$; ****$P<0.001$.

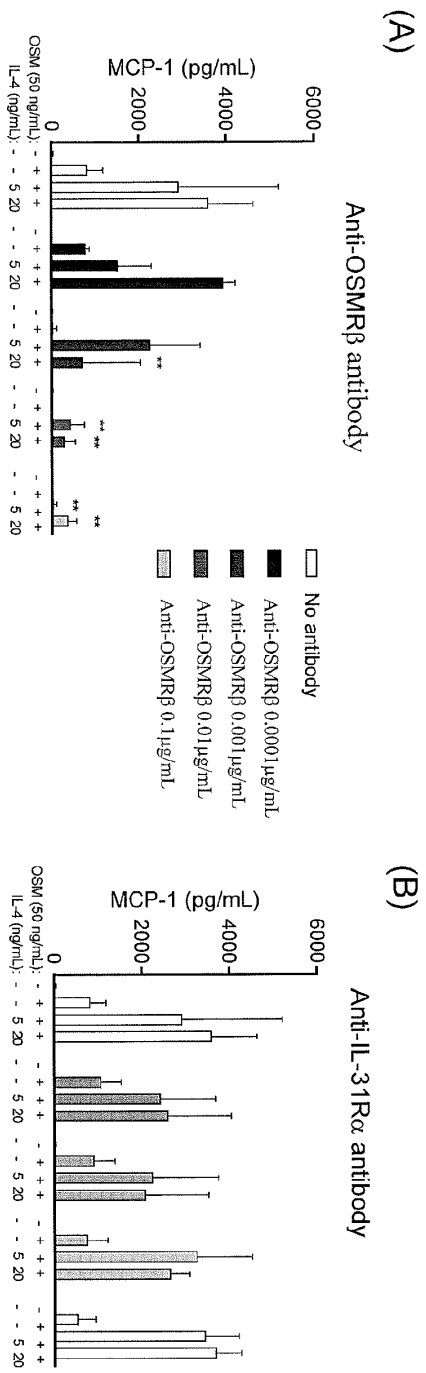
FIGURE 14



Data are mean ± SEM; two-way ANOVA; $^{**}P<0.01$, no antibody vs OSMRβ at concentration of 0.001–0.1 µg/mL.

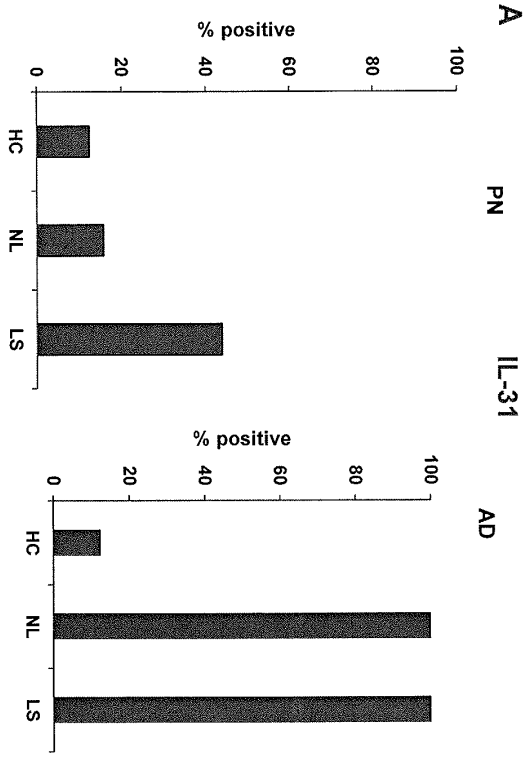
CCL2 = monocyte chemoattractant protein-1 (**MCP**-1); Anti-IL-31Rα = humanized antihuman interleukin-31 receptor A antibody; HEK = human epidermal keratinocytes; IL = interleukin; LIF = leukemia inhibitory factor; OSM = oncostatin M; RNA = ribonucleic acid.

FIGURE 15



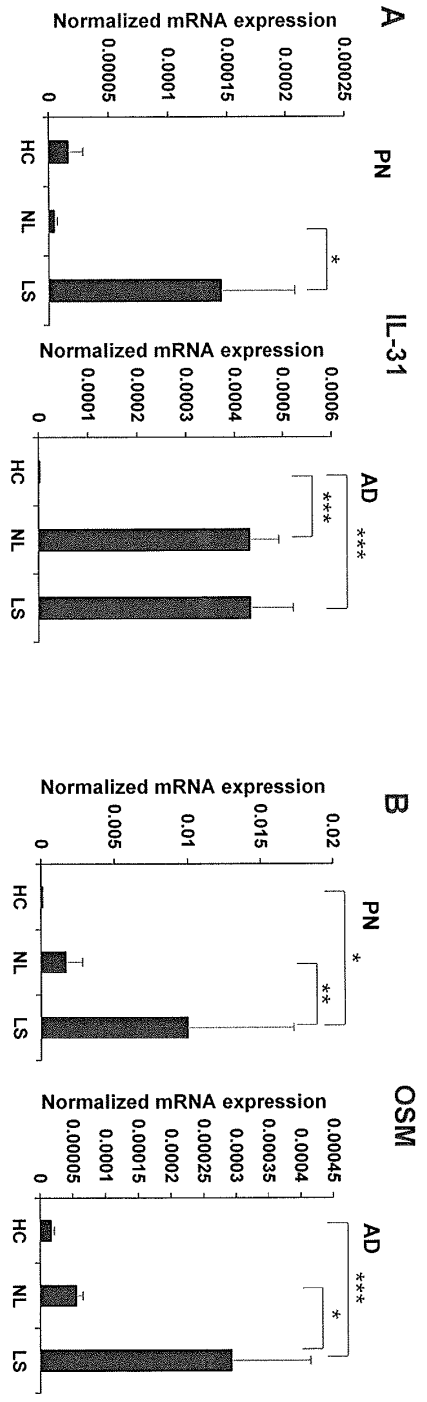
Data are mean ± SEM; two-way ANOVA; $^{**}P<0.01$, no antibody vs OSMRβ.
CCL2 = monocyte chemoattractant protein-1 (MCP-1); Anti-IL-31Rα = humanized antihuman interleukin-31 receptor A antibody; HEK = human epidermal keratinocytes; IL = interleukin; OSM = oncostatin M.

FIGURE 16



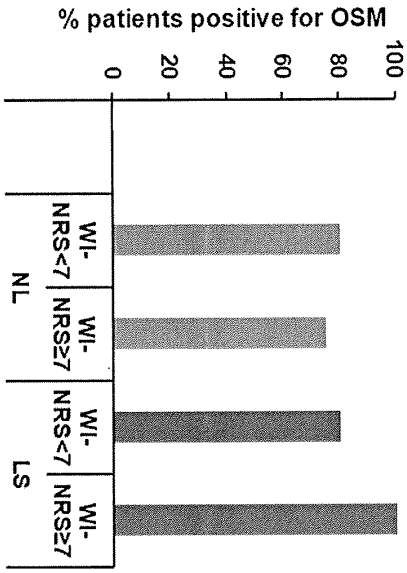
PN: prurigo nodularis, AD: atopic dermatitis, HC: healthy control, NL: non-lesional, LS: lesional,. PN: HC n=16, NL n=19, LS n=41; AD: HC n=16, NL n=28, LS n=32.

FIGURE 17



PN: prurigo nodularis, AD: atopic dermatitis, HC: healthy control, NL: non-lesional, LS: lesional. PN: HC n=16, NL n=19, LS n=41; AD: HC n=16, NL n=28, LS n=32; *p<0.05, **p<0.01, ***p<0.005

FIGURE 18



NL: non-lesional, LS: lesional, WI-NRS: Worst Itch Numeric Rating Scale. NL: WI-NRS<7 n=11, WI-NRS ≥7 n=8; LS: WI-NRS<7 n=27, WI-NRS ≥7 n=14.

FIGURE 19

B

IL-31

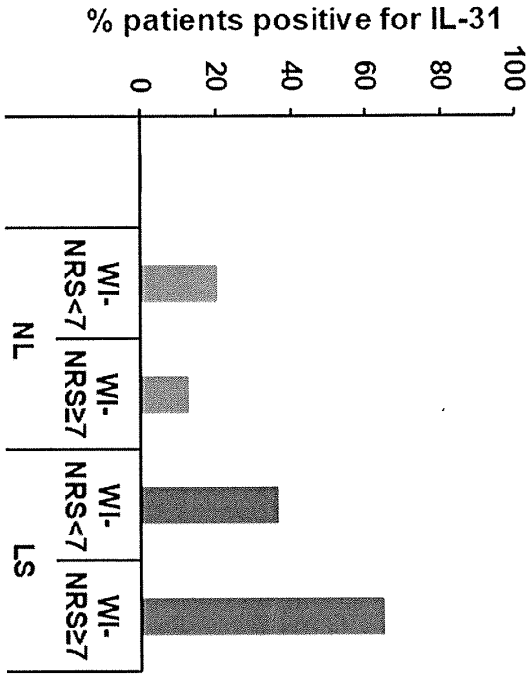


FIGURE 19, continued

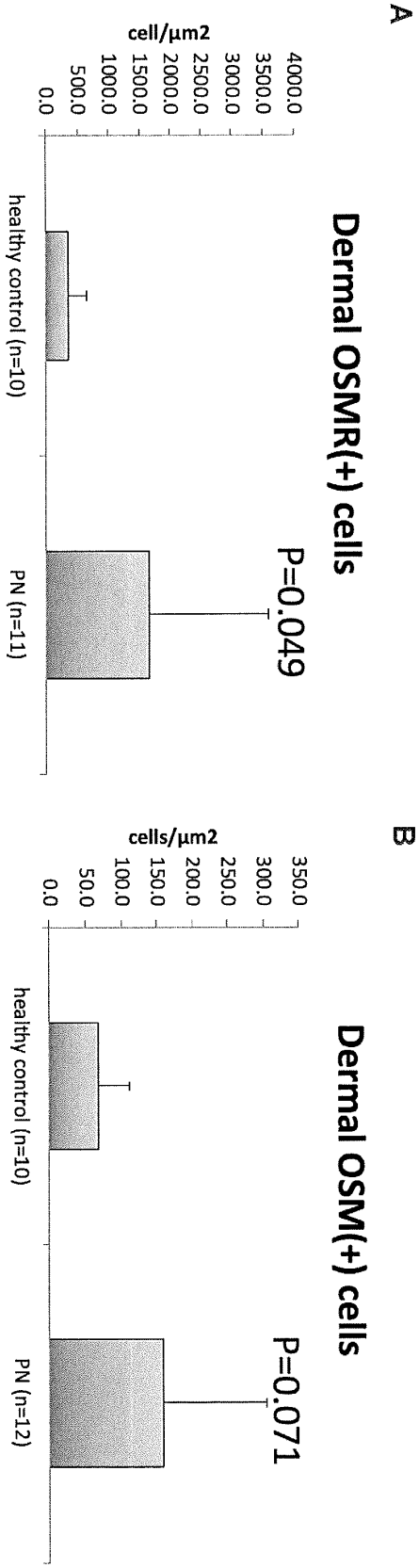

A
Dermal OSMR(+) cells
cell/µm2
4000.0
3500.0
3000.0
2500.0
2000.0
1500.0
1000.0
500.0
0.0
healthy control (n=10)
PN (n=11)
P=0.049
B
Dermal OSM(+) cells
cells/µm2
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
healthy control (n=10)
PN (n=12)
P=0.071

FIGURE 20

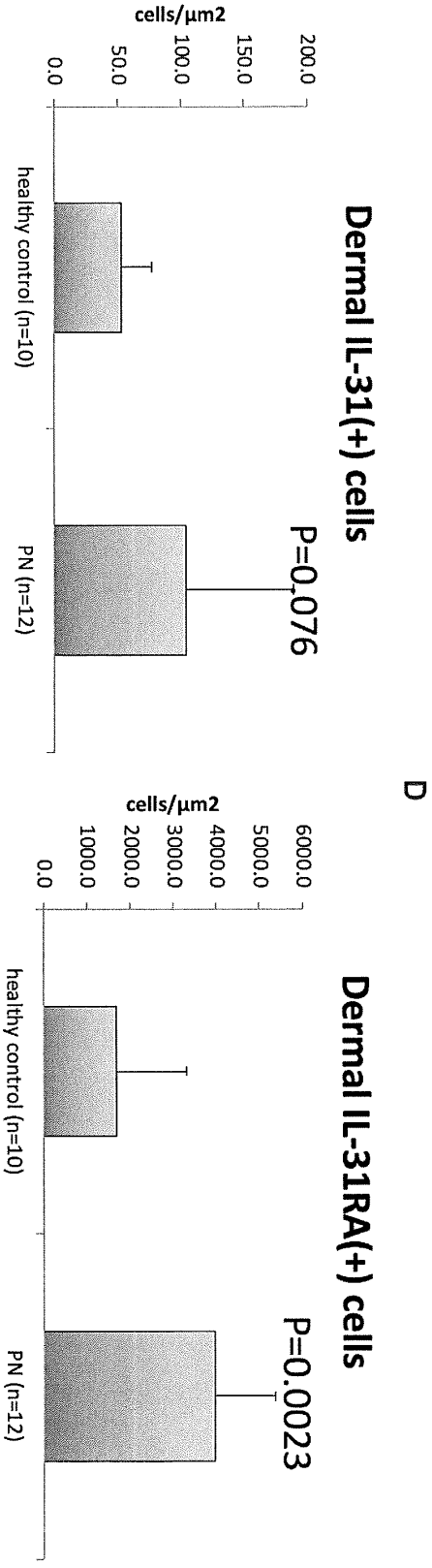
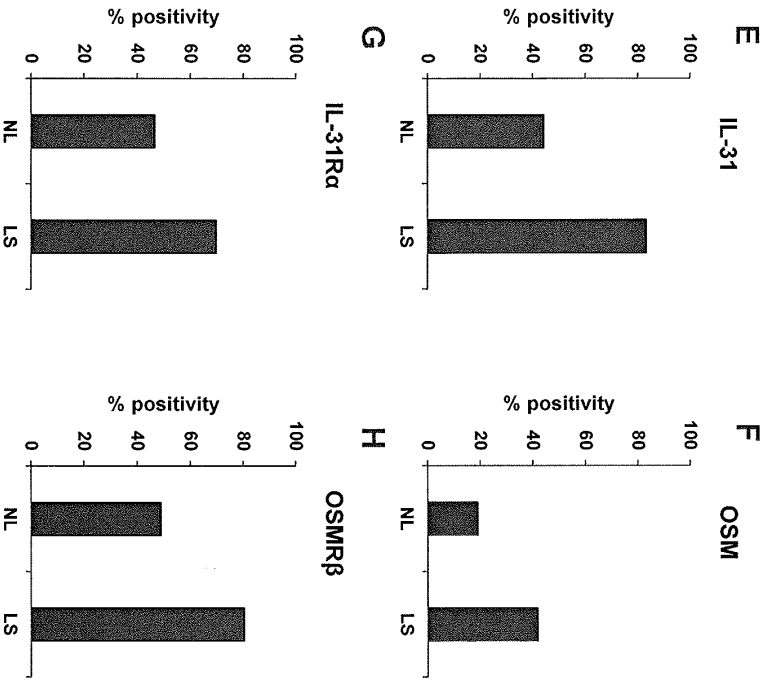


FIGURE 20, continued



NL: non-lesional, LS: lesional,. PN: HC n=16, NL n=19, LS n=41.

FIGURE 20, continued

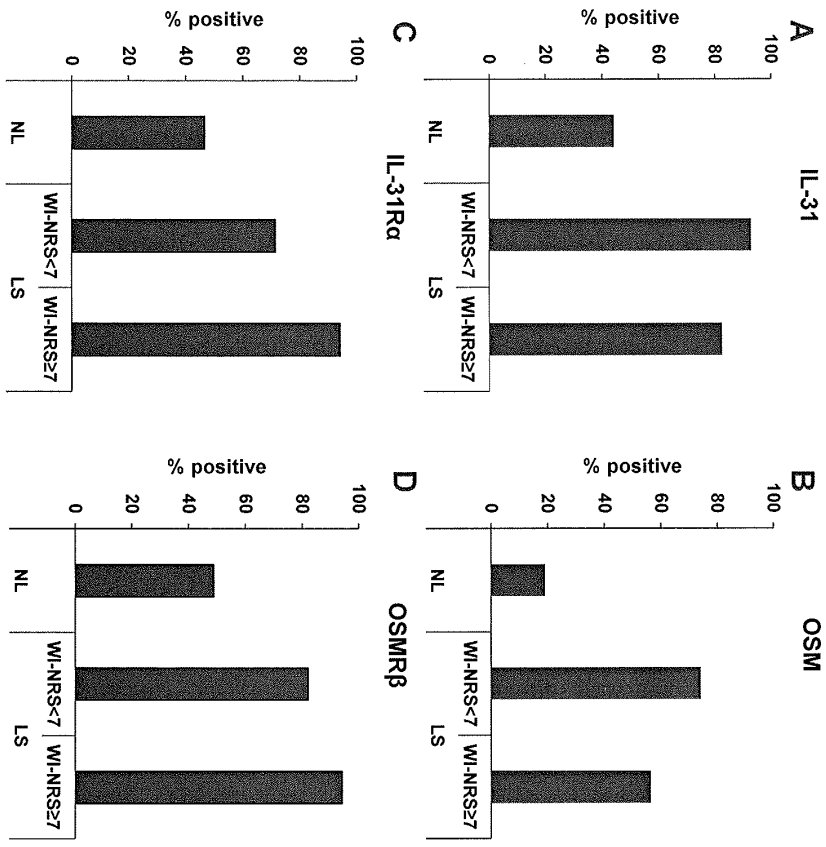

A
IL-31
% positive
0
20
40
60
80
100
NL
LS
WI-NRS<7
WI-NRS≥7
B
OSM
C
IL-31Rα
D
OSMRβ

FIGURE 21

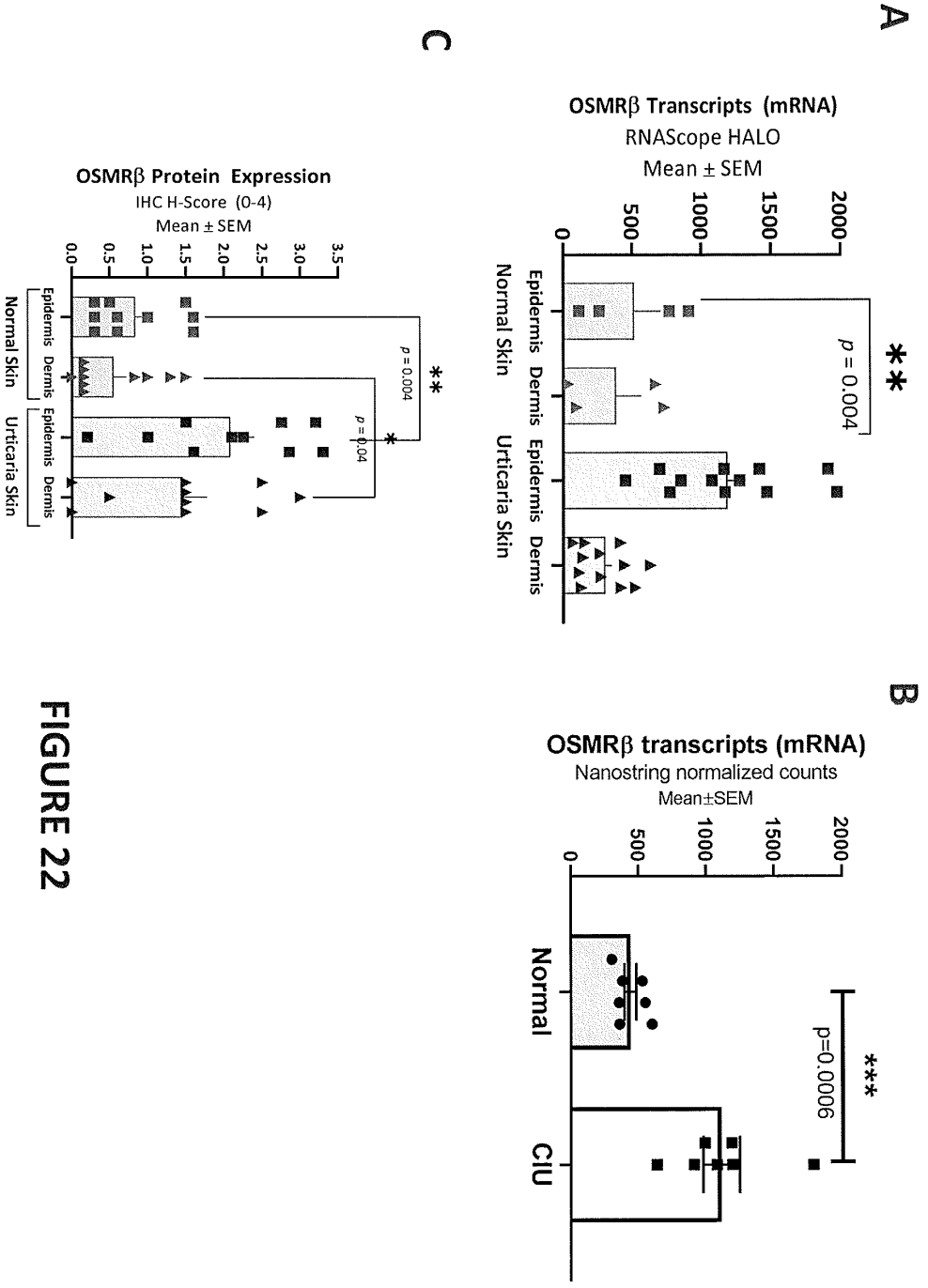

A
OSMRβ Transcripts (mRNA)
RNAScope HALO
Mean ± SEM
0
500
1000
1500
2000
p = 0.004
**
Epidermis
Dermis
Epidermis
Dermis
Normal Skin
Urticaria Skin
B
OSMRβ transcripts (mRNA)
Nanostring normalized counts
Mean±SEM
0
500
1000
1500
2000
p=0.0006
***
Normal
CIU
C
OSMRβ Protein Expression
IHC H-Score (0-4)
Mean ± SEM
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
p = 0.004
**
p = 0.04
*
Epidermis
Dermis
Epidermis
Dermis
Normal Skin
Urticaria Skin

FIGURE 22

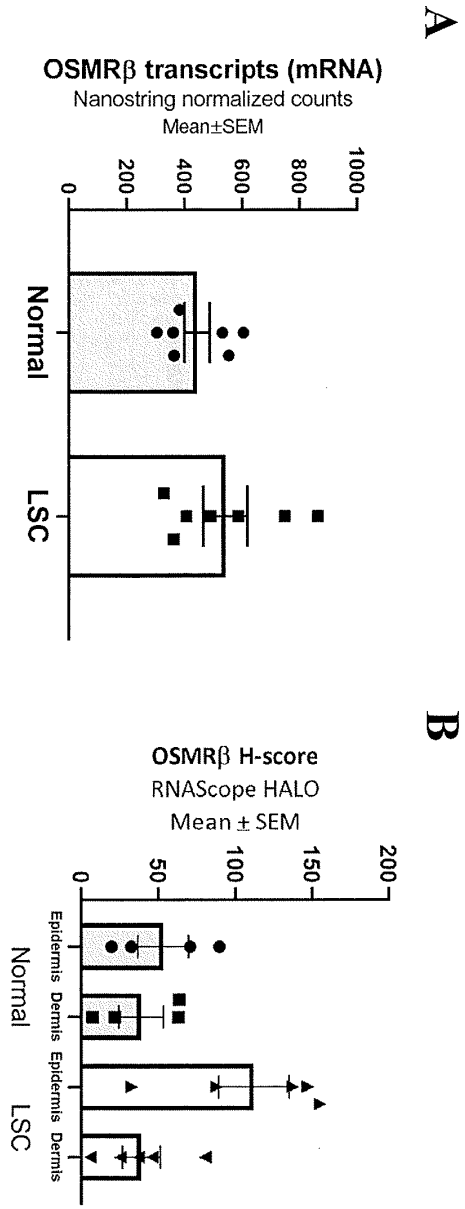

A
OSMRβ transcripts (mRNA)
Nanostring normalized counts
Mean±SEM
0
200
400
600
800
1000
Normal
LSC
B
OSMRβ H-score
RNAScope HALO
Mean ± SEM
0
50
100
150
200
Epidermis
Dermis
Epidermis
Dermis
Normal
LSC

FIGURE 23

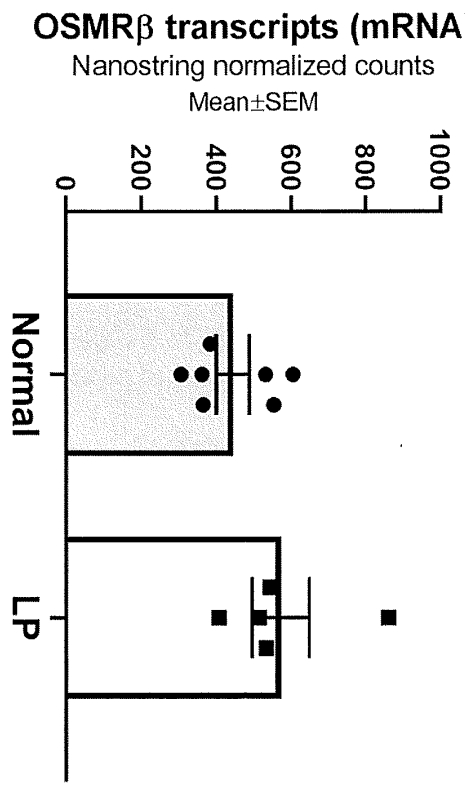

OSMRβ transcripts (mRNA)
Nanostring normalized counts
Mean±SEM
0
200
400
600
800
1000
Normal
LP

FIGURE 24

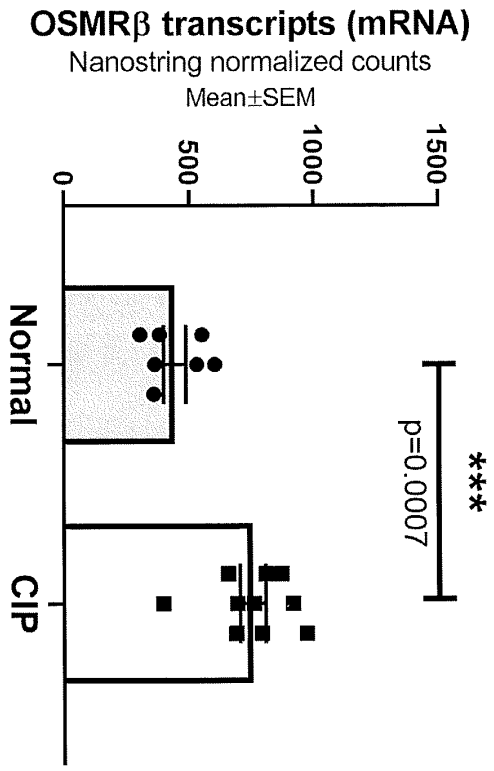

OSMRβ transcripts (mRNA)
Nanostring normalized counts
Mean±SEM
0
500
1000
1500
Normal
CIP
p=0.0007
***

FIGURE 25