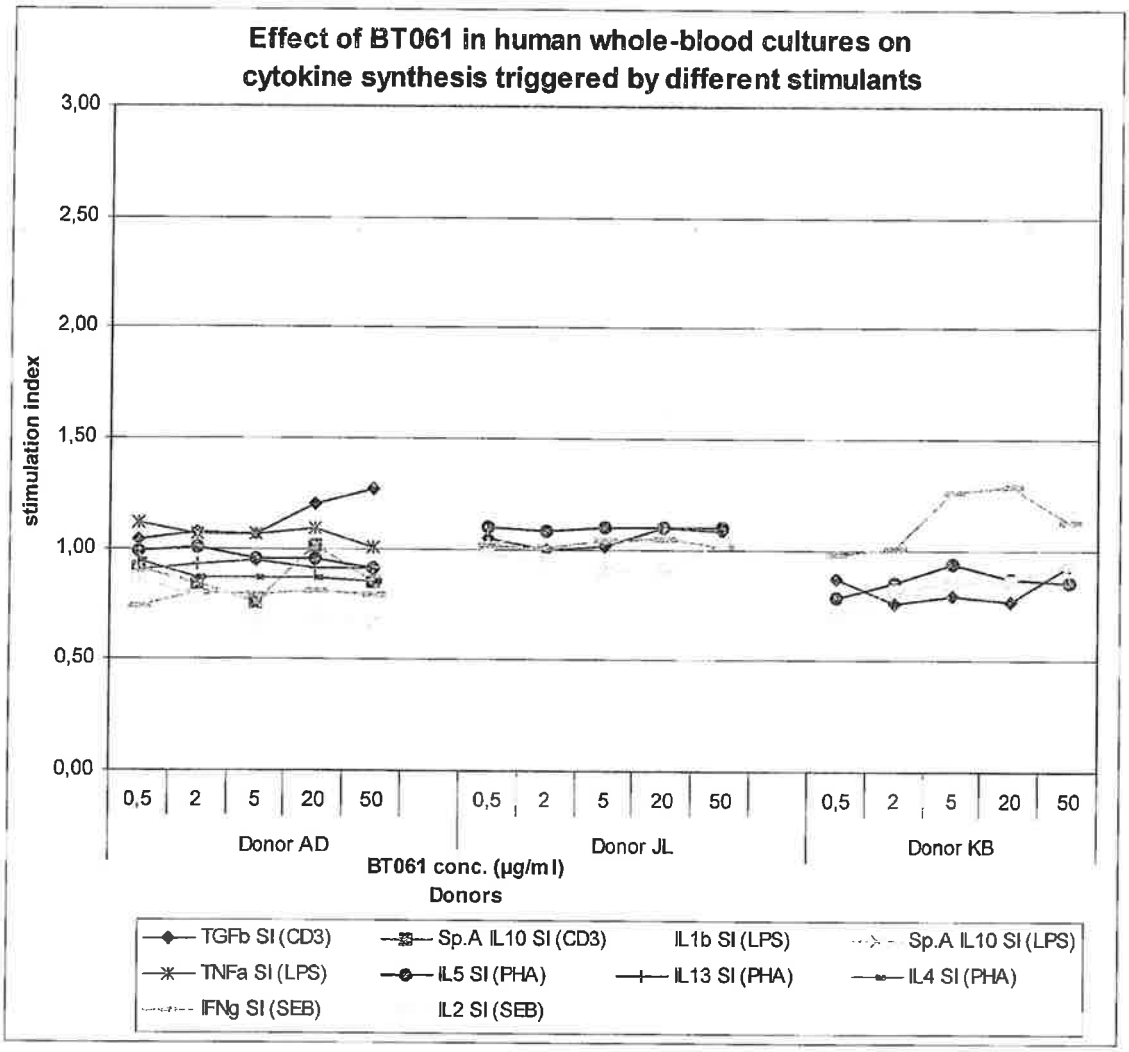

Effect of BT061 in human whole-blood cultures on cytokine synthesis triggered by different stimulants
stimulation index
3,00
2,50
2,00
1,50
1,00
0,50
0,00
0,5
2
5
20
50
Donor AD
Donor JL
Donor KB
BT061 conc. (µg/ml)
Donors
TGFb SI (CD3)
Sp.A IL10 SI (CD3)
IL1b SI (LPS)
Sp.A IL10 SI (LPS)
TNFa SI (LPS)
IL5 SI (PHA)
IL13 SI (PHA)
IL4 SI (PHA)
IFNg SI (SEB)
IL2 SI (SEB)

FIGURE 1

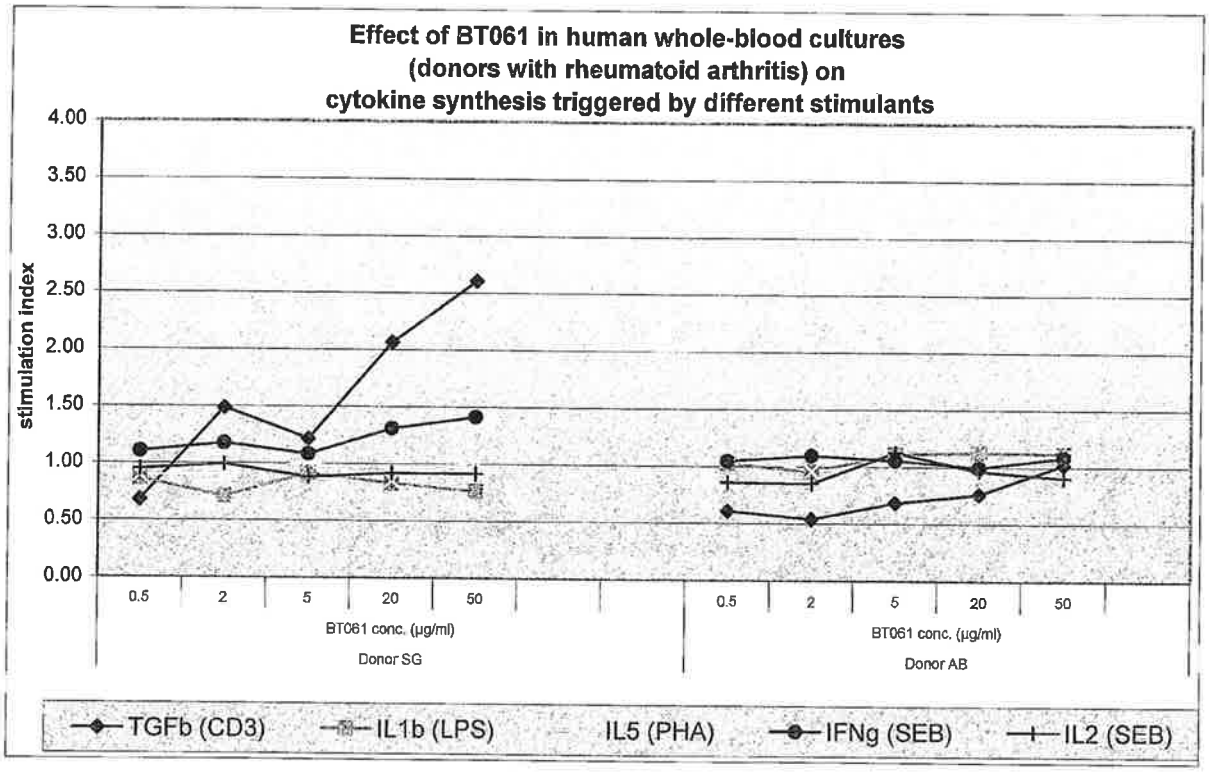

Effect of BT061 in human whole-blood cultures
(donors with rheumatoid arthritis) on
cytokine synthesis triggered by different stimulants
stimulation index
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.5
2
5
20
50
BT061 conc. (µg/ml)
Donor SG
0.5
2
5
20
50
BT061 conc. (µg/ml)
Donor AB
TGFb (CD3)
IL1b (LPS)
IL5 (PHA)
IFNg (SEB)
IL2 (SEB)

FIGURE 2

mB-F5 V_H

CAG GAA TAC CTT GTG GAG ACC GGG GGA GGC TTG GTG AGG CCT GGA AAT TCT CTG AAA

CTC TCC TGT GTC ACC TCG GGT TTC AGT TTC AGT GAC TGC CGG ATG TAC TGG CTT CGC

CAG CCT CCA GGG AAG GGG CTG GAG TGG ATT GGT GTG ATT TCA GTC AAA TCT GAG AAT

TAT GGA GCA AAT TAT GCA GAG TCT GTG AGG GGC AGA TTC ACT ATT TCA AGA GAT GAT

TCA AAA AGC AGT GTC TAT CTG CAG ATG AGC AGA TTG AGA GAG GAA GAC ACT GCC ACT

TAT TAT TGT AGT GCC TCC TAT TAT AGG TAC GAC GTG GGG GCC TGG TTT GCT TAC TGG

GGC CAA GGG ACT CTG GTC ACT GTC TCT GCA

FIGURE 3

mB-F5 V_K

GAC ATT GTG CTG ACA CAG TCT CCT TCT TCC TTA GTT GTA TCT CTG GGG CAG AGG GCC

ACC ATC TCA TGC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAC AGT TAT ATA TAT

TGG TAC CAA CAG ATC CCA GGA CAG CCA CCC AAA CTC CTC ATC TAT CTT GCA TCC ATC

CTA GAA TCT GGG GTC CCT GGC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC

CTC AAC ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC AGT

AGG GAA CTT CCG TGG ACG TTC GGT GGA GGC ACC AAG CTG GAG ATC AAA CGG GCT GAT

GCT GCA CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT GAG CA

FIGURE 4

```
GA GGA GCT CCA GAC AAT GTC TGT CTC CTT CCT CAT CTT CCT GCC CGT GCT GGG CCT

CCC ATG GGG TCA GTG TCA GGG AGA TGC CGT ATT CAC AGC AGC ATT CAC AGA CTG AGG

GGT GTT TCA CTT TGC TGT TTC CTT TTG TCT CCA GGT GTC CTG TCA GAG GAA CAG CTT
                                                            E   E   Q   L

GTG GAG TCT GGG GGA GGC TTG GTG AAA CCC GGA GGT TCT CTG AGG CTC TCC TGT GCA
 V   E   S   G   G   G   L   V   K   P   G   G   S   L   R   L   S   C   A

GCC TCG GGT TTC AGT TTC AGT GAC TGC CGG ATG TAC TGG GTT CGC CAG GCT CCA GGG
 A   S   G   F   S   F   S   D   C   R   M   Y   W   V   R   Q   A   P   G

AAG GGG CTG GAG TGG ATT GGT GTG ATT TCA GTC AAA TCT GAG AAT TAT GGA GCA AAT
 K   G   L   E   W   I   G   V   I   S   V   K   S   E   N   Y   G   A   N

TAT GCA GAG TCT GTG AGG GGC AGA TTC ACT ATT TCA AGA GAT GAT TCA AAA AAC ACG
 Y   A   E   S   V   R   G   R   F   T   I   S   R   D   D   S   K   N   T

GTC TAT CTG CAG ATG AAC AGC TTG AAG ACC GAA GAC ACT GCC GTT TAT TAT TGT AGT
 V   Y   L   Q   M   N   S   L   K   T   E   D   T   A   V   Y   Y   C   S

GCC TCC TAT TAT AGG TAC GAC GTG GGG GCC TGG TTT GCT TAC TGG GGC CAA GGG ACT
 A   S   Y   Y   R   Y   D   V   G   A   W   F   A   Y   W   G   Q   G   T

CTG GTC ACT GTC TCT TCA GGT AAG AAT GGC CAA GCT TG
 L   V   T   V   S   S
```

FIGURE 5

```
GGA GGA TCC AAT TAT CTG CTG ACT TAT AAT ACT ACT AGA AAG CAA ATT TAA ATG ACA

TAT TTC AAT TAT ATC TGA GAC AGC GTG TAT AAG TTT ATG TAT AAT CAT TGT CCA TTC

CTG ACT ACA GGT GCC TAC GGG GAC ATC GTG ATG ACC CAG TCT CCA GAC TCC CTG GCT
                              D   I   V   M   T   Q   S   P   D   S   L   A

GTG TCT CTG GGC GAG AGG GCC ACC ATC AAC TGC AGG GCC AGC AAA AGT GTC AGT ACA
 V   S   L   G   E   R   A   T   I   N   C   R   A   S   K   S   V   S   T

TCT GGC TAC AGT TAT ATA TAT TGG TAC CAG CAG AAA CCA GGA CAG CCT CCT AAG CTG
 S   G   Y   S   Y   I   Y   W   Y   Q   Q   K   P   G   Q   P   P   K   L

CTC ATT TAC CTT GCA TCC ATC CTA GAA TCT GGG GTC CCT GAC CGA TTC AGT GGC AGC
 L   I   Y   L   A   S   I   L   E   S   G   V   P   D   R   F   S   G   S

GGG TCT GGG ACA GAT TTC ACT CTC ACC ATC AGC AGC CTG CAG GCT GAA GAT GTG GCA
 G   S   G   T   D   F   T   L   T   I   S   S   L   Q   A   E   D   V   A

GTT TAT TAC TGT CAG CAC AGT AGG GAA CTT CCG TGG ACG TTC GGC CAA GGG ACC AAG
 V   Y   Y   C   Q   H   S   R   E   L   P   W   T   F   G   Q   G   T   K

GTG GAA ATC AAA CGT GAG TAG AAT TTA AAT TTT AAG CTT CTT
 V   E   I   K
```

FIGURE 6

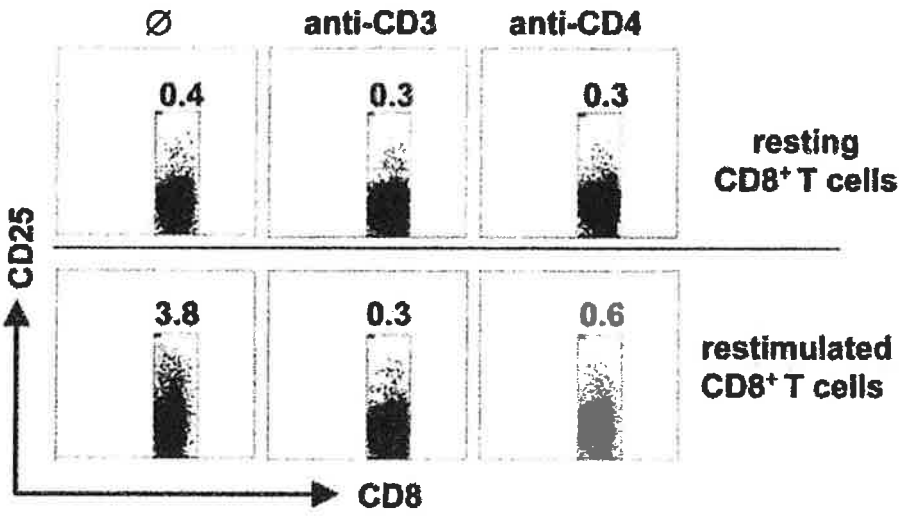

∅
anti-CD3
anti-CD4
0.4
0.3
0.3
resting
CD8+ T cells
CD25
3.8
0.3
0.6
restimulated
CD8+ T cells
CD8

FIGURE 7

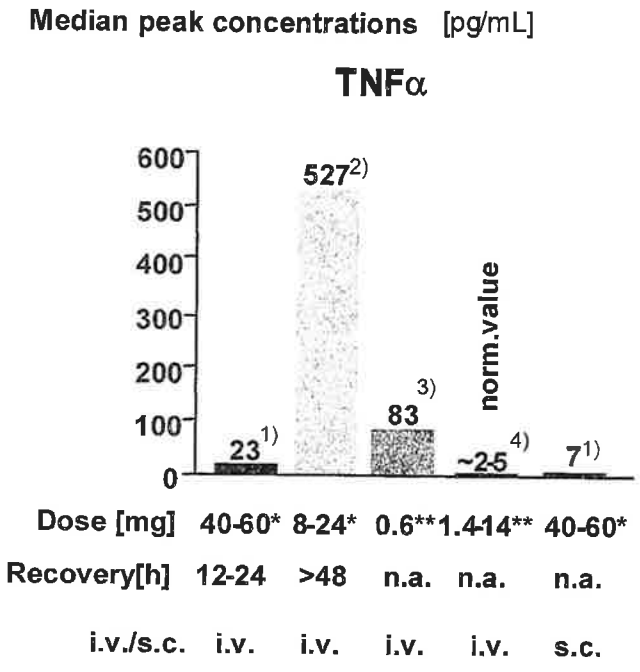


FIGURE 8A

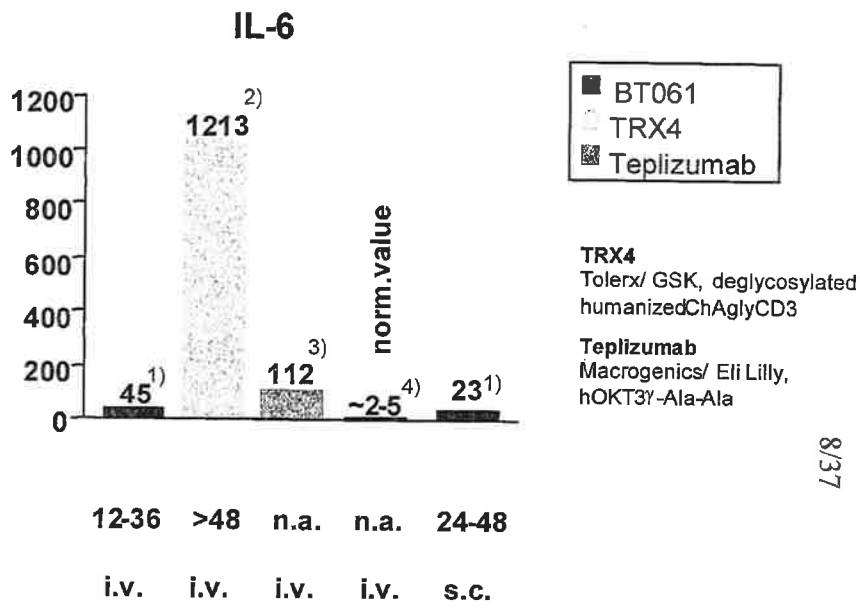


FIGURE 8B

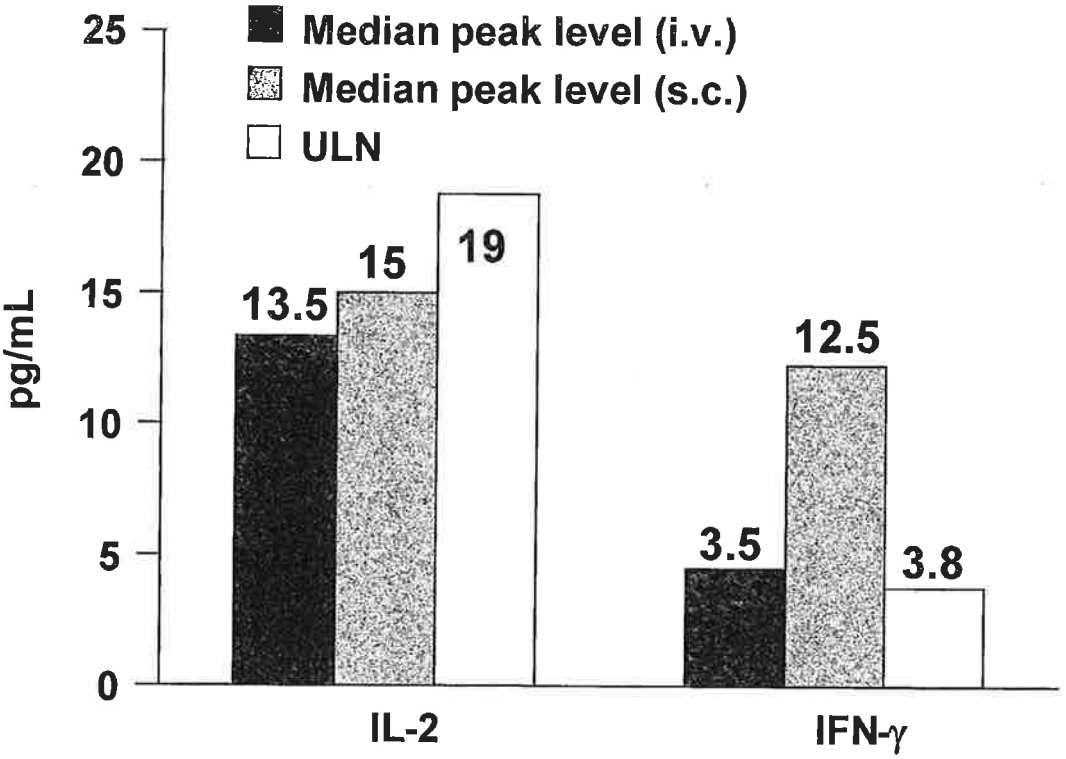

Median peak level (i.v.)
Median peak level (s.c.)
ULN
pg/mL
25
20
15
10
5
0
13.5
15
19
3.5
12.5
3.8
IL-2
IFN-γ

FIGURE 9

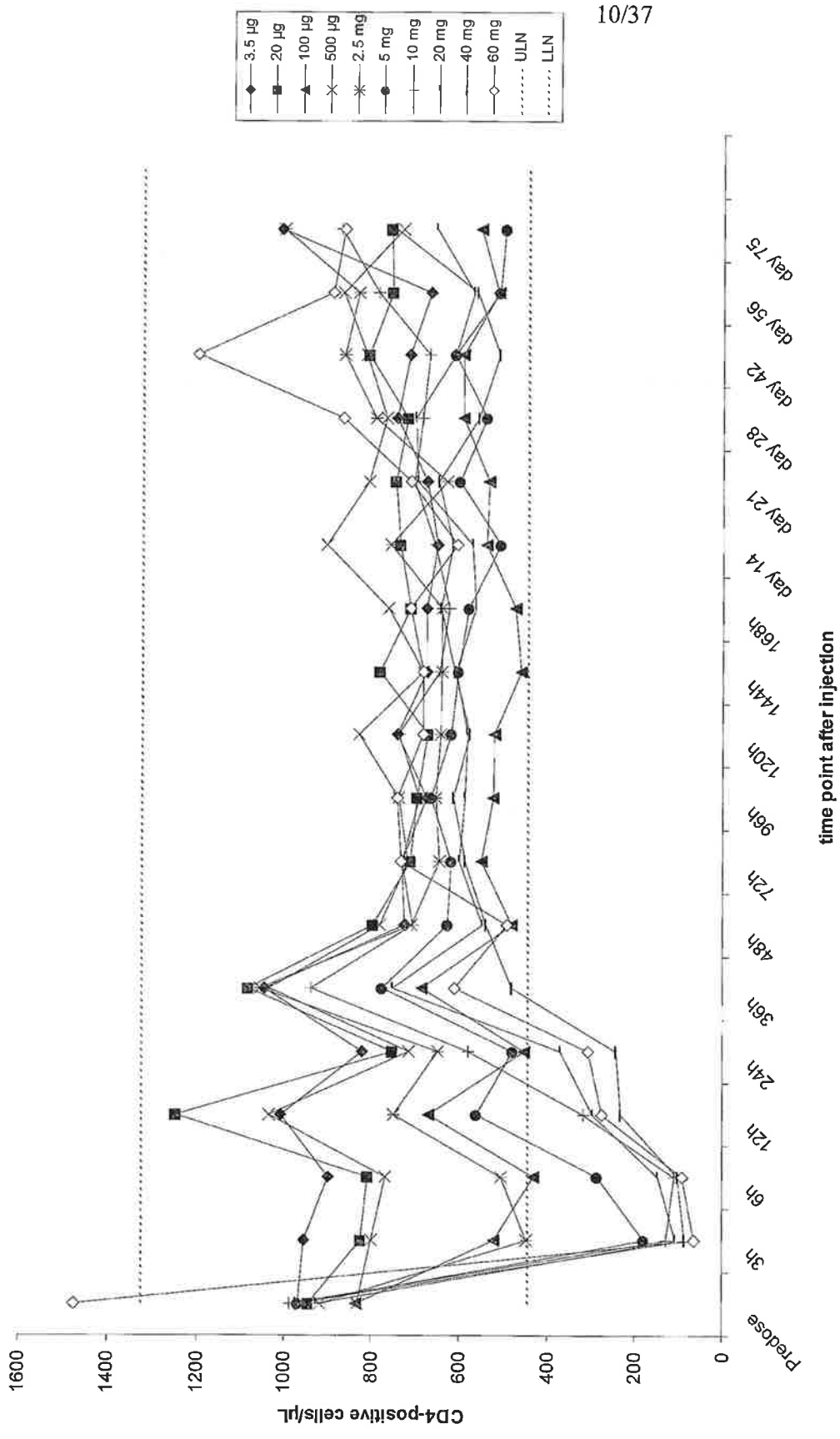

3.5 µg
20 µg
100 µg
500 µg
2.5 mg
5 mg
10 mg
20 mg
40 mg
60 mg
ULN
LLN
CD4-positive cells/µL
0
200
400
600
800
1000
1200
1400
1600
predose
3h
6h
12h
24h
36h
48h
72h
96h
120h
144h
168h
day 14
day 21
day 28
day 42
day 56
day 75
time point after injection

FIGURE 10

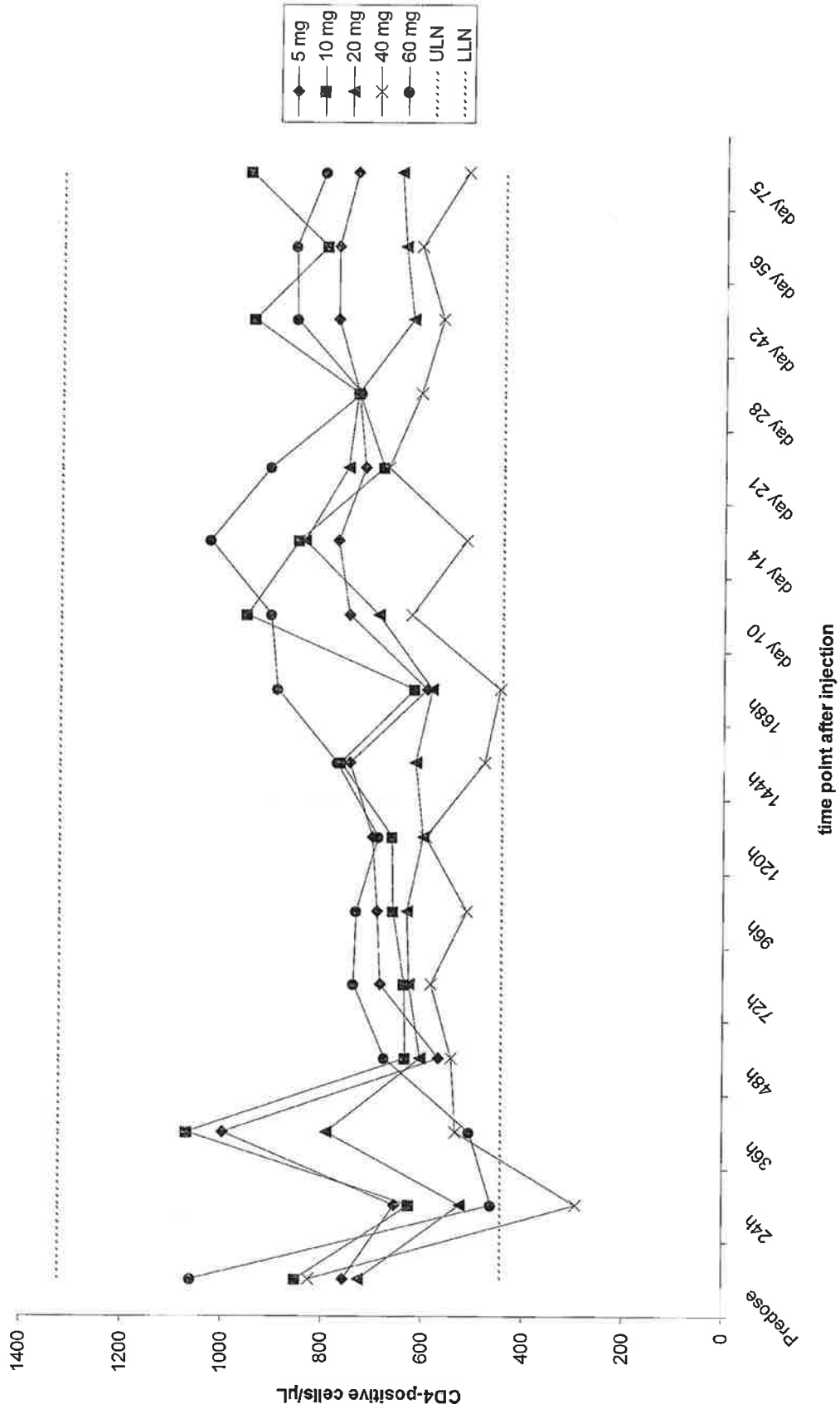

5 mg
10 mg
20 mg
40 mg
60 mg
ULN
LLN
CD4-positive cells/µL
1400
1200
1000
800
600
400
200
0
predose
24h
36h
48h
72h
96h
120h
144h
168h
day 10
day 14
day 21
day 28
day 42
day 56
day 75
time point after injection

FIGURE 11

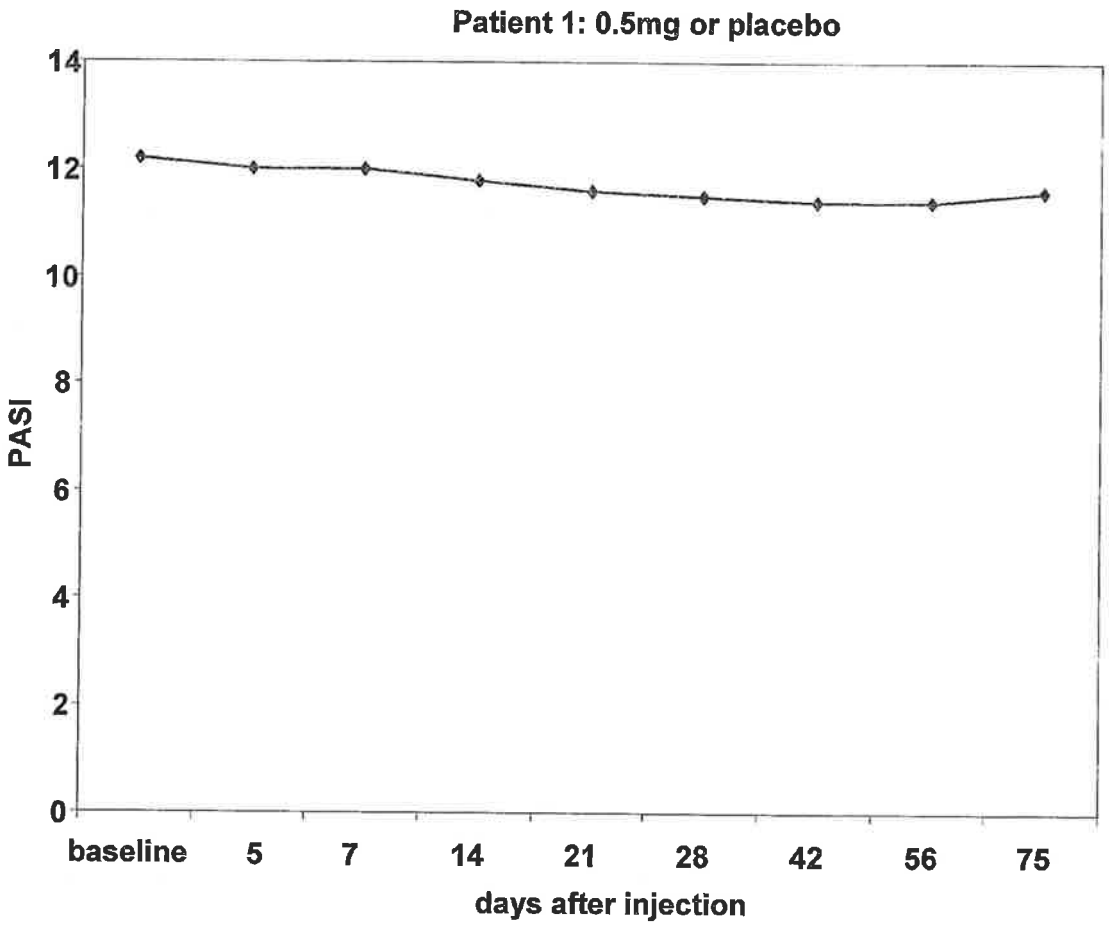

Patient 1: 0.5mg or placebo
PASI
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12A

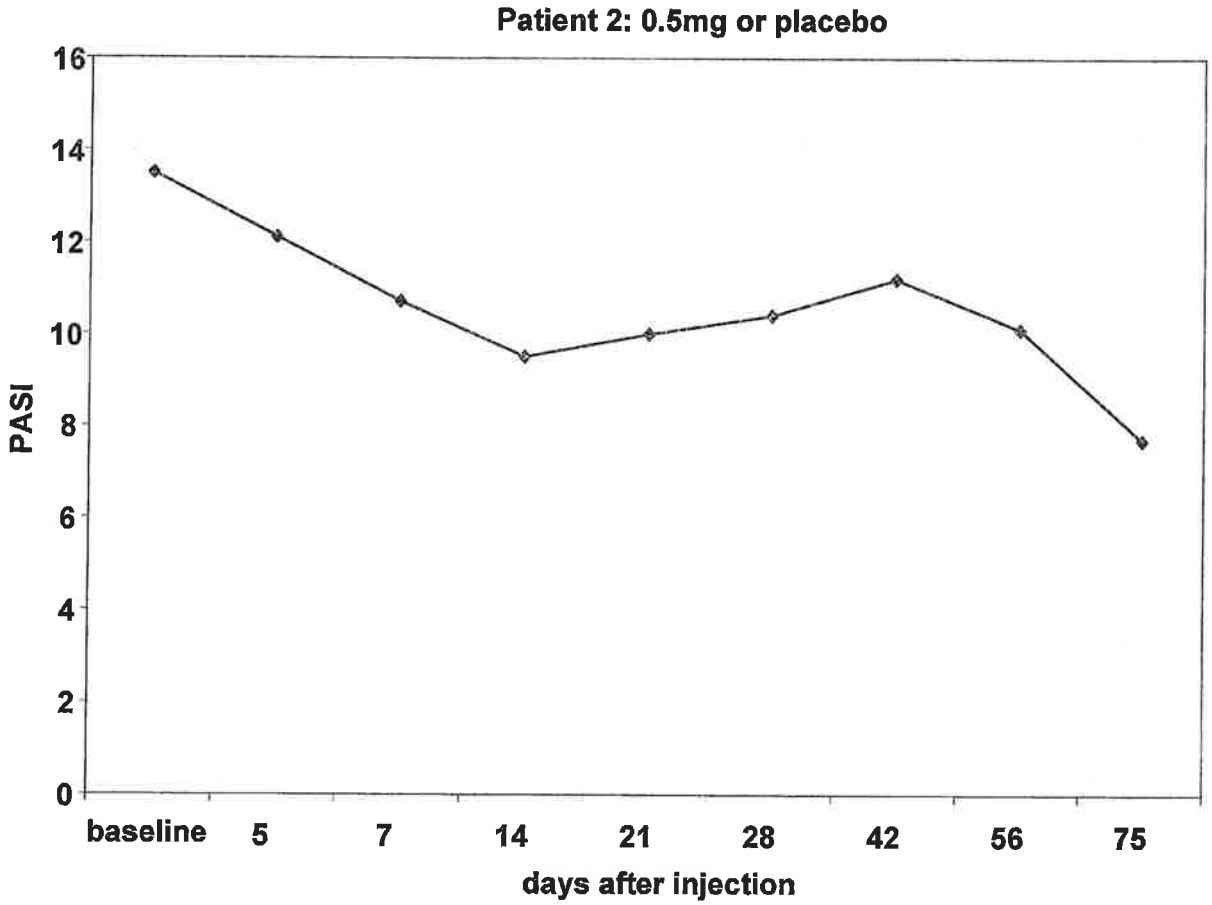

Patient 2: 0.5mg or placebo
PASI
16
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12B

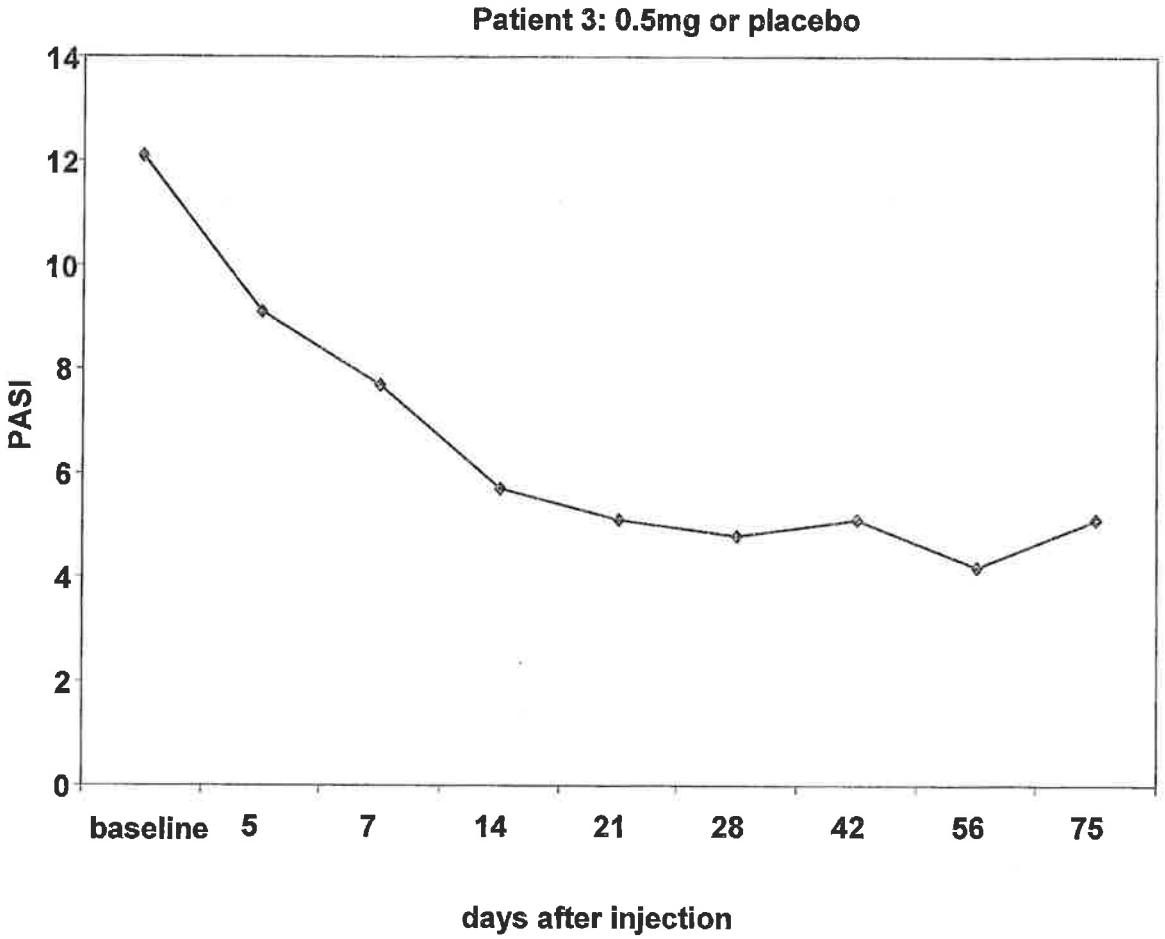

Patient 3: 0.5mg or placebo
PASI
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12C

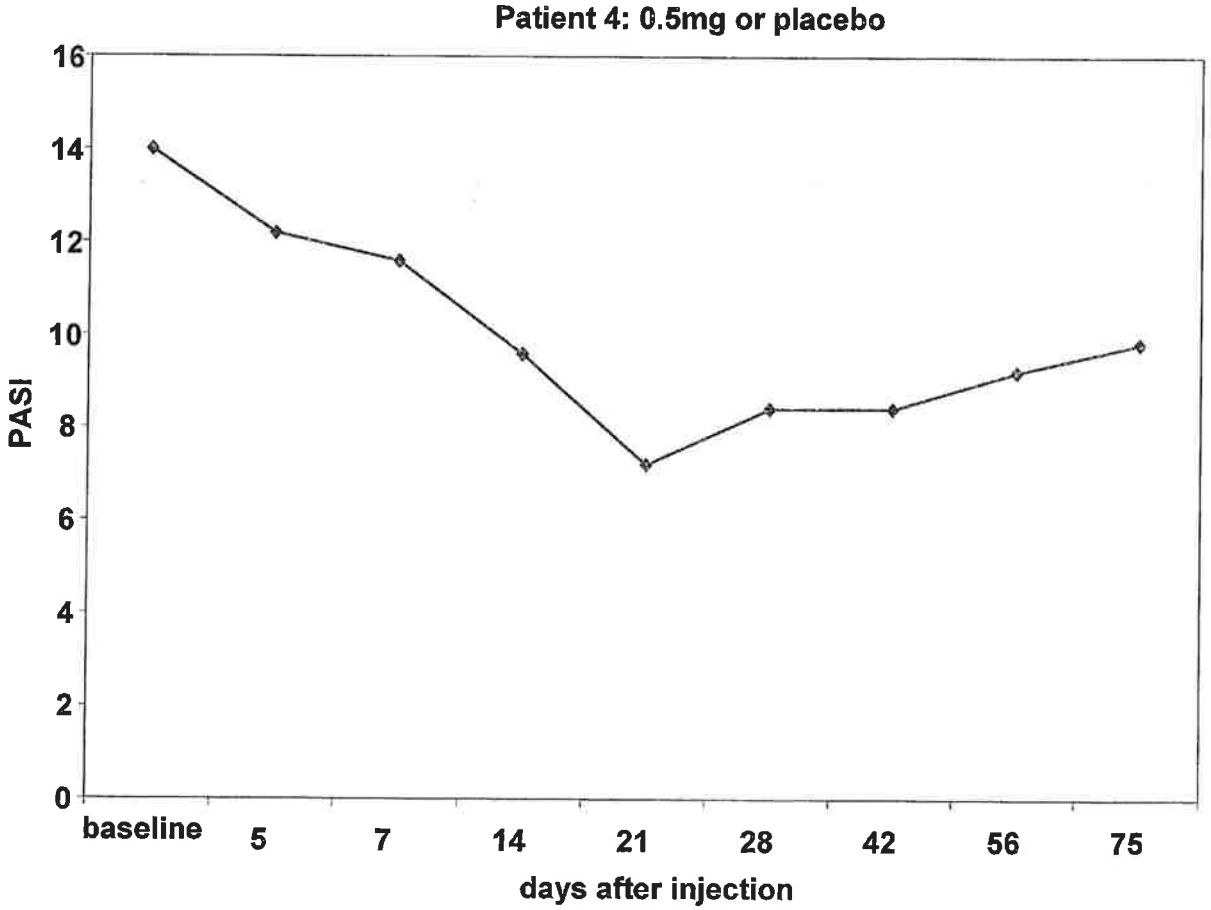

Patient 4: 0.5mg or placebo
PASI
16
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12D

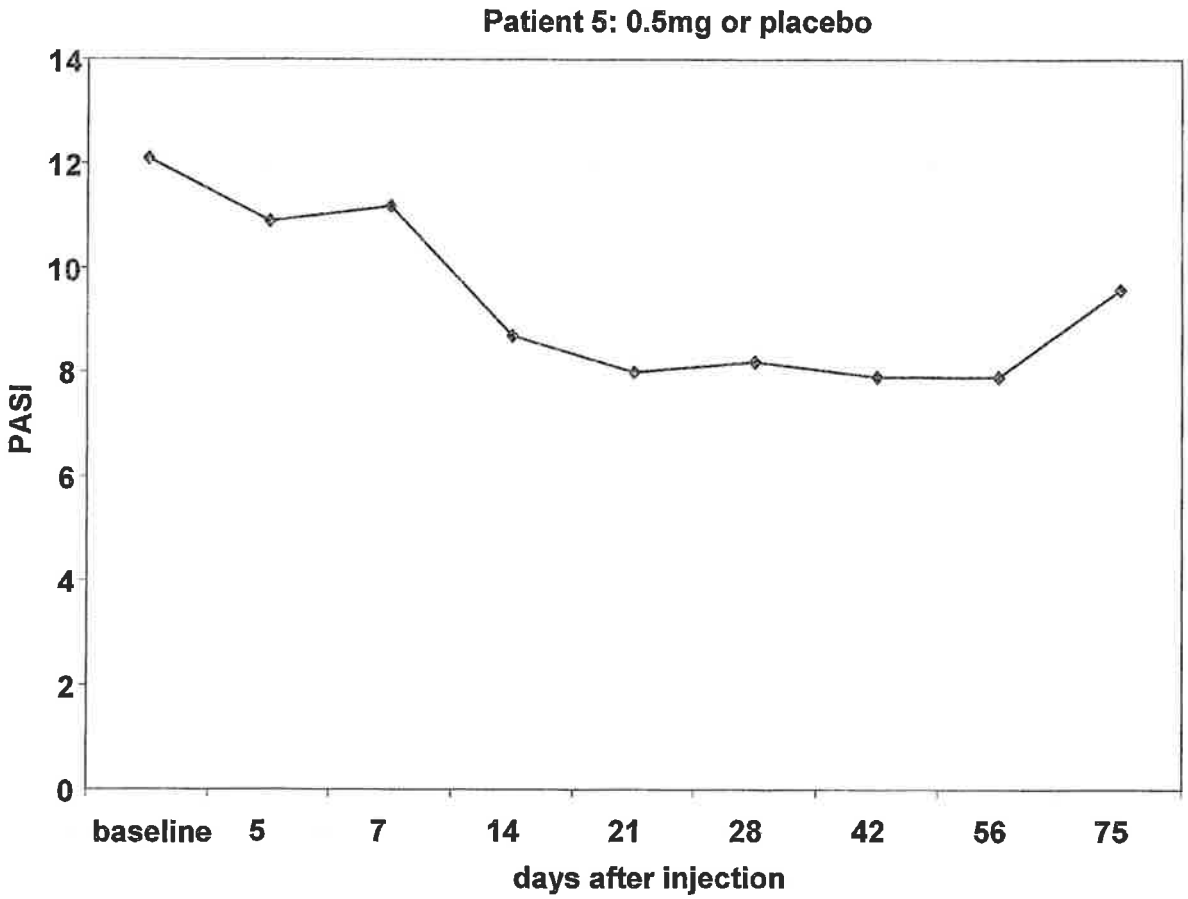

Patient 5: 0.5mg or placebo
PASI
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12E

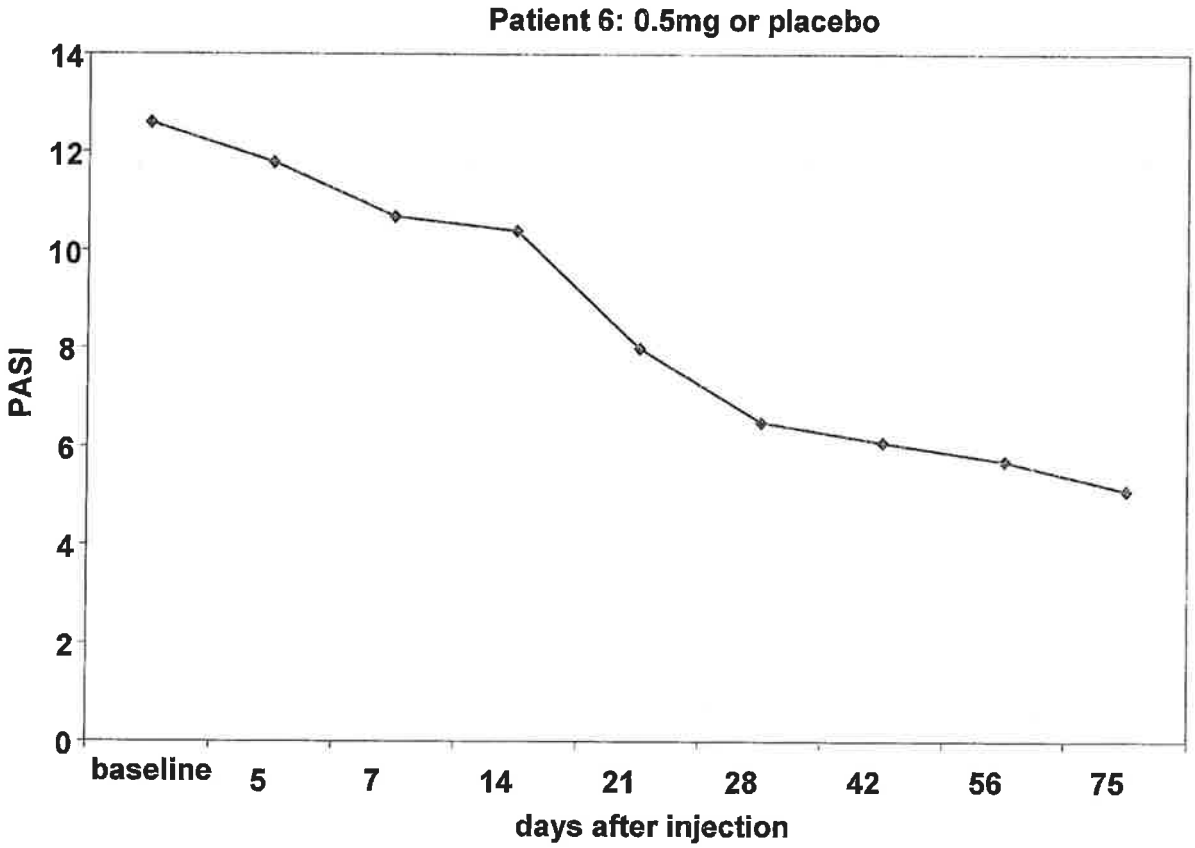

Patient 6: 0.5mg or placebo
PASI
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12F

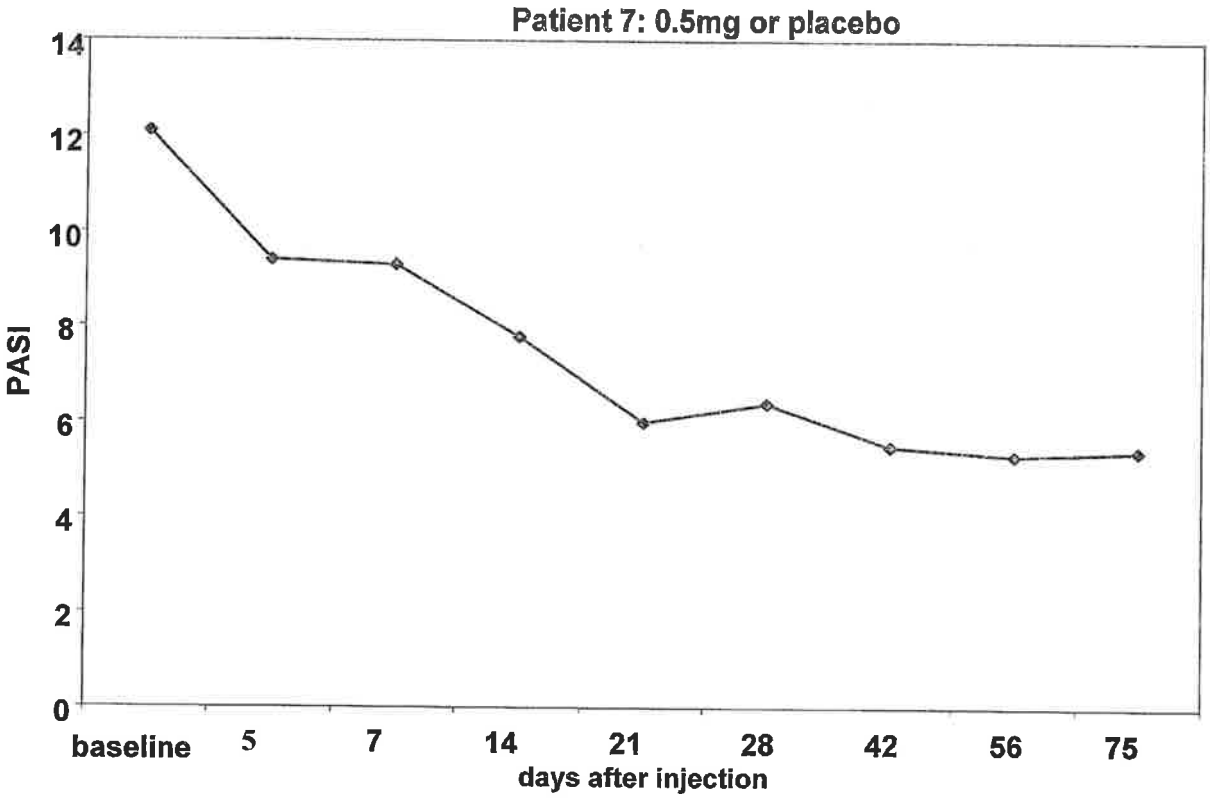

Patient 7: 0.5mg or placebo
PASI
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12G

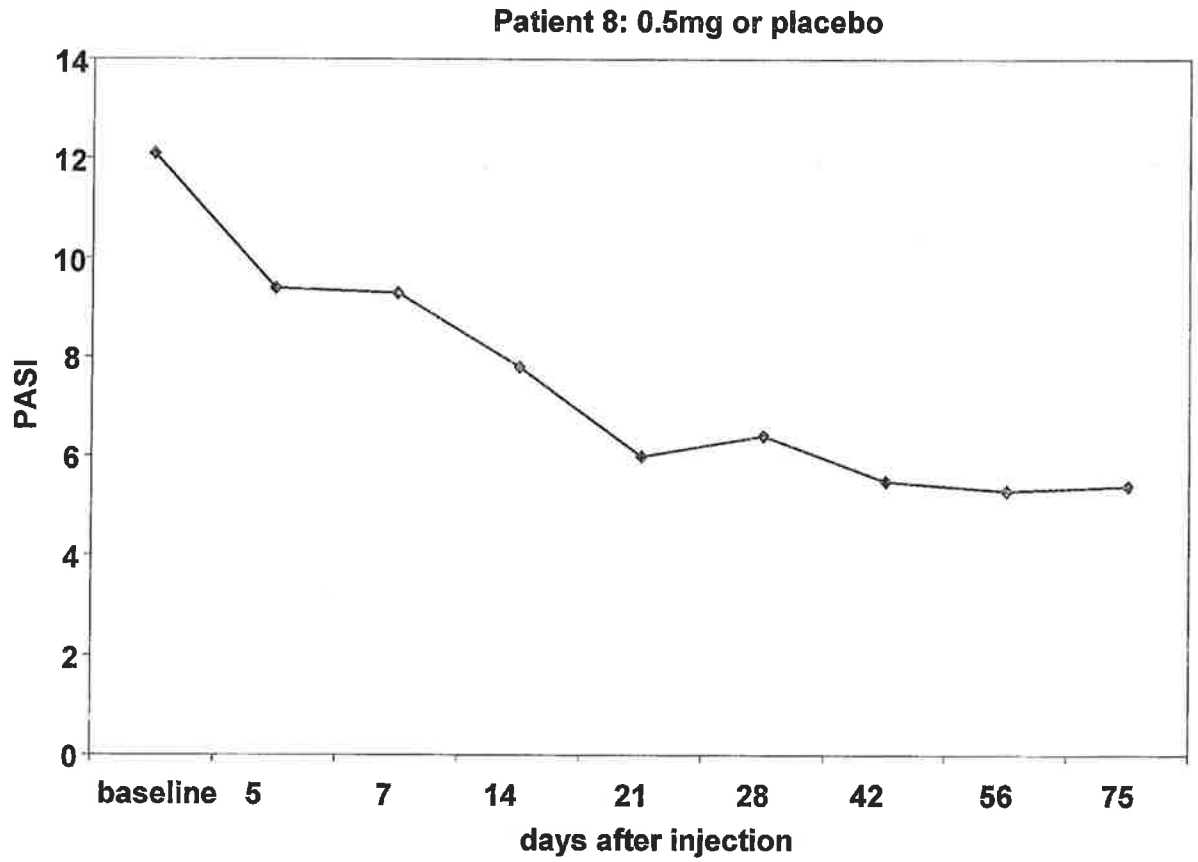

Patient 8: 0.5mg or placebo
PASI
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 12H

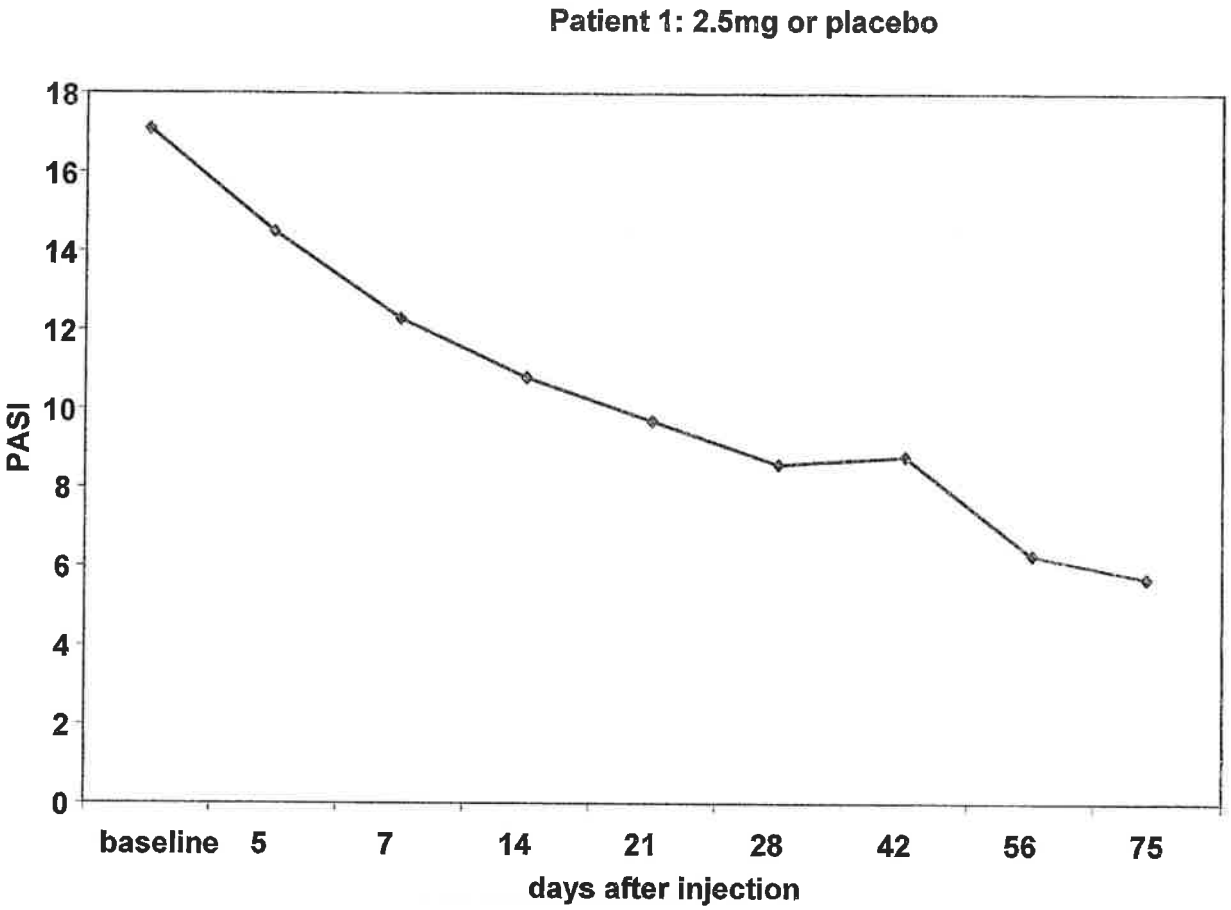

Patient 1: 2.5mg or placebo
PASI
18
16
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13A

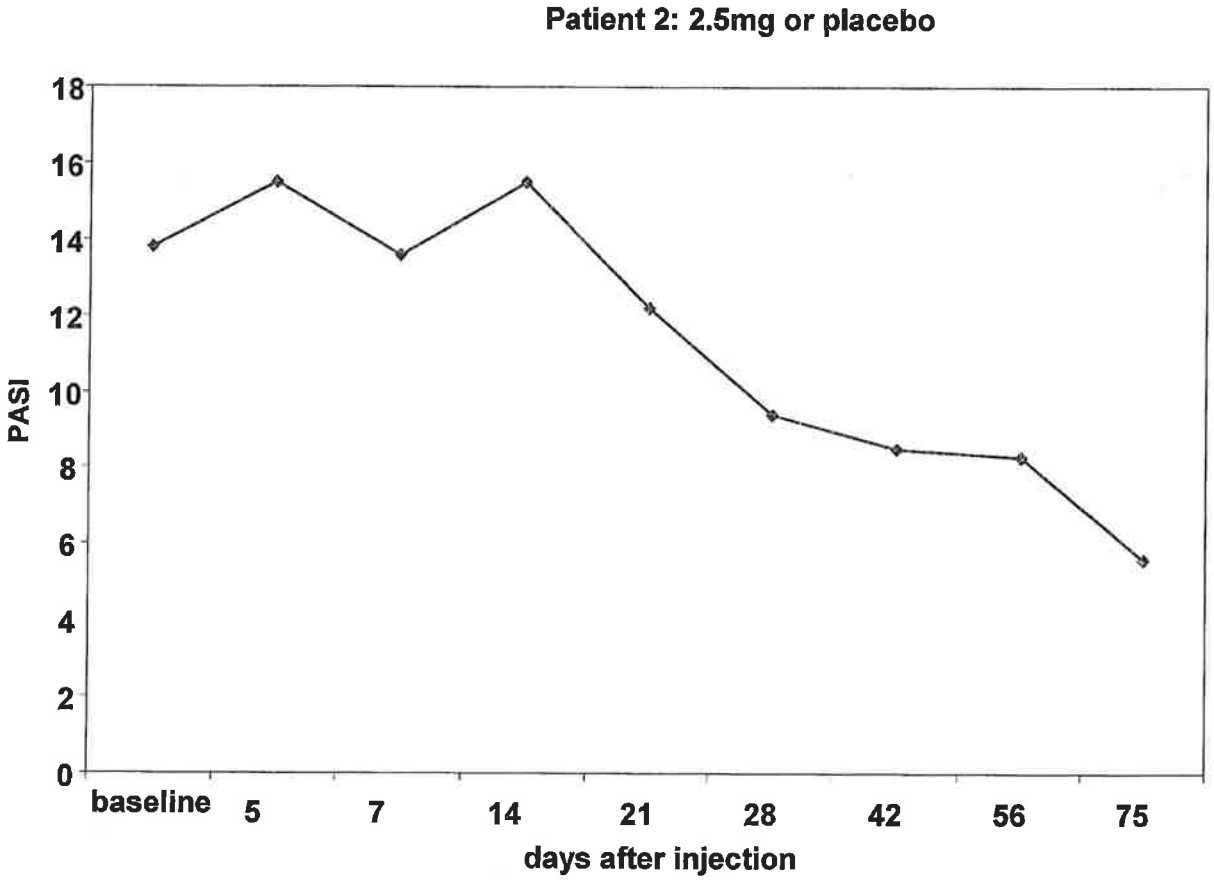

Patient 2: 2.5mg or placebo
PASI
18
16
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13B

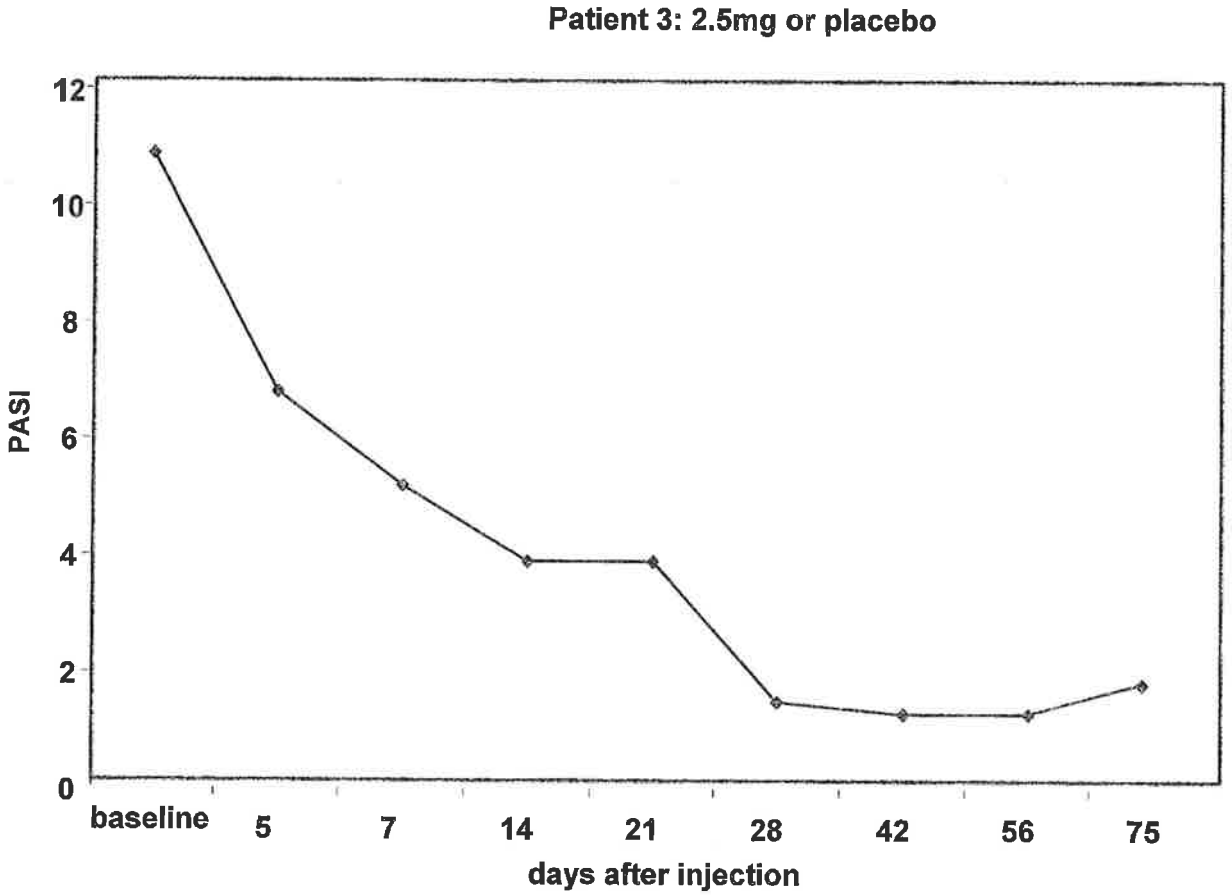

Patient 3: 2.5mg or placebo
PASI
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13C

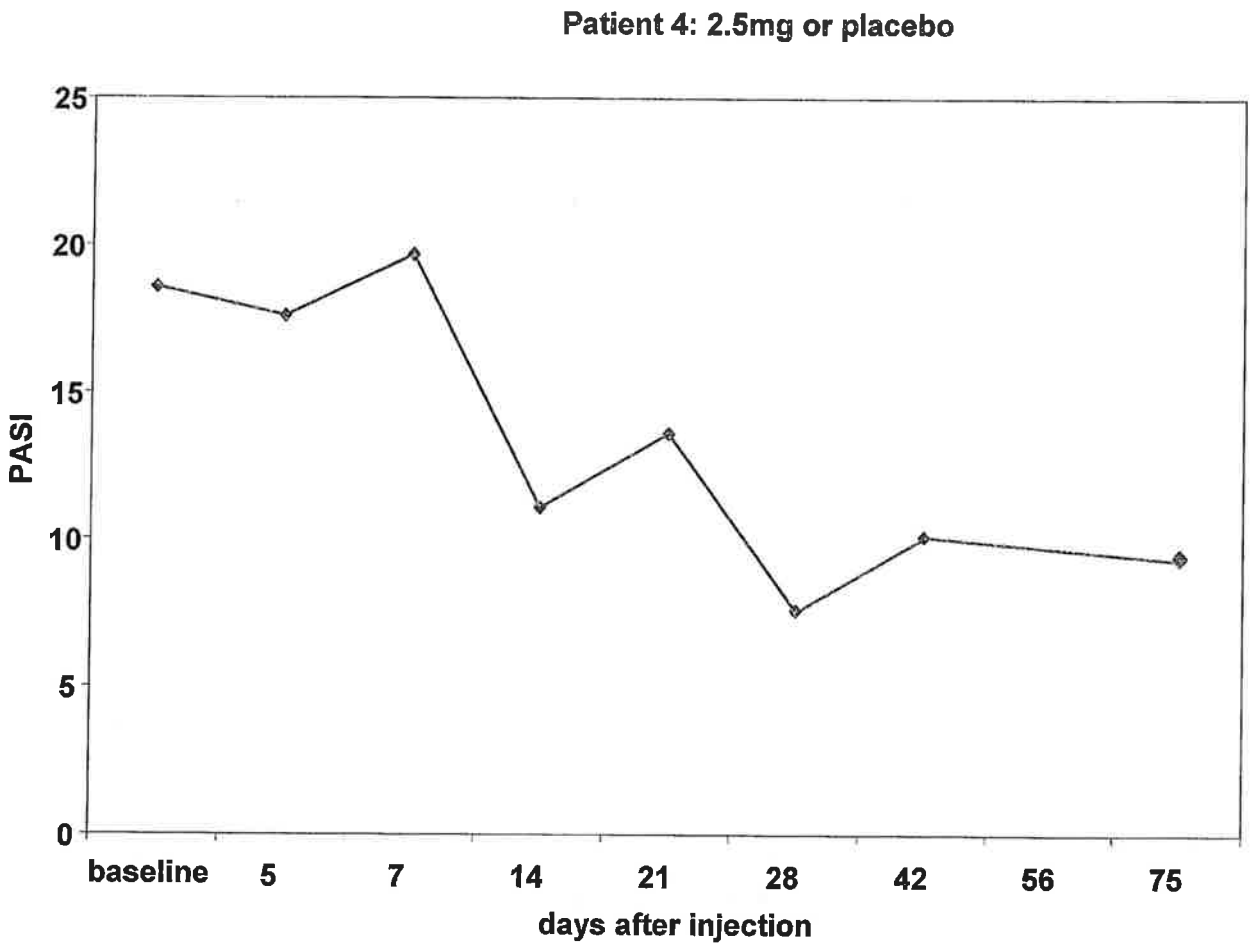

Patient 4: 2.5mg or placebo
PASI
25
20
15
10
5
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13D

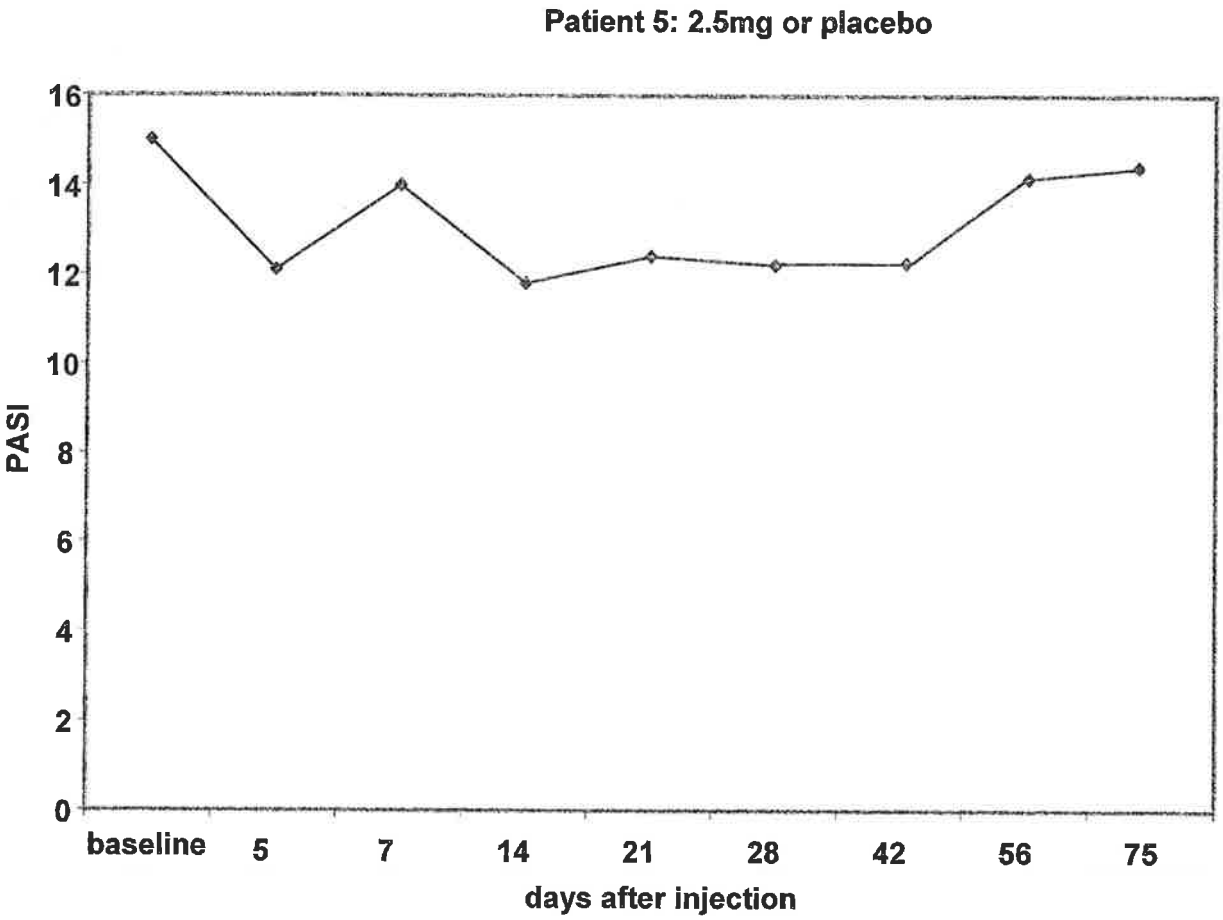

Patient 5: 2.5mg or placebo
16
14
12
10
8
6
4
2
0
PASI
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13E

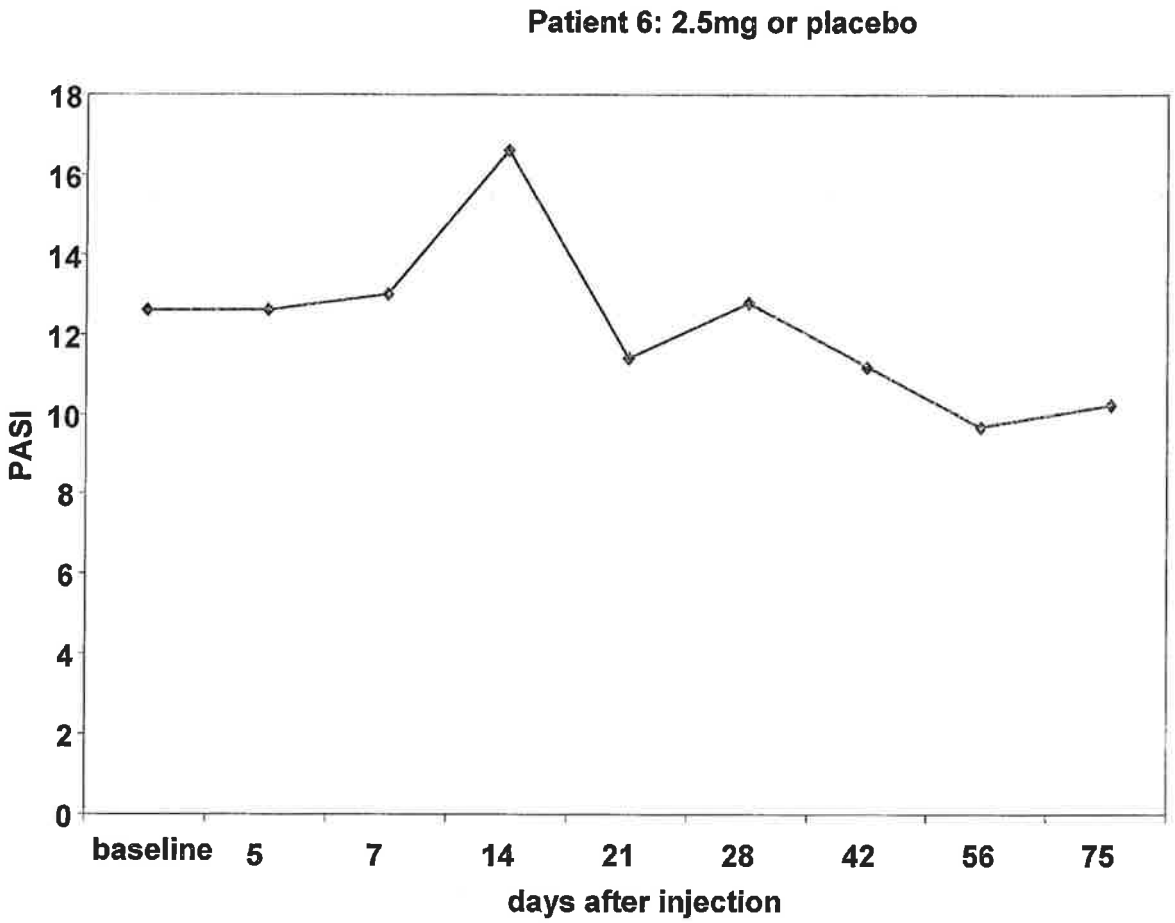

Patient 6: 2.5mg or placebo
PASI
18
16
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13F

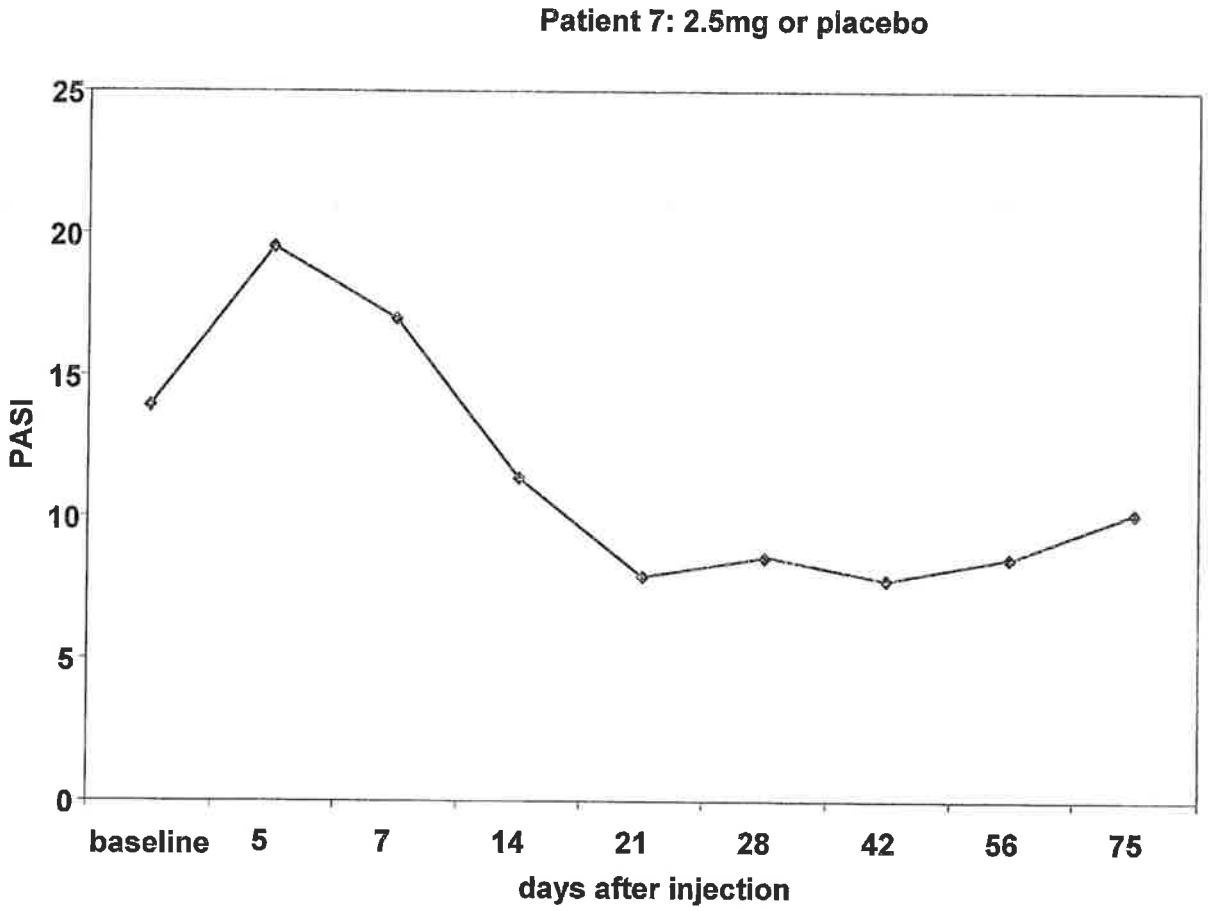

Patient 7: 2.5mg or placebo
25
20
15
10
5
0
PASI
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13G

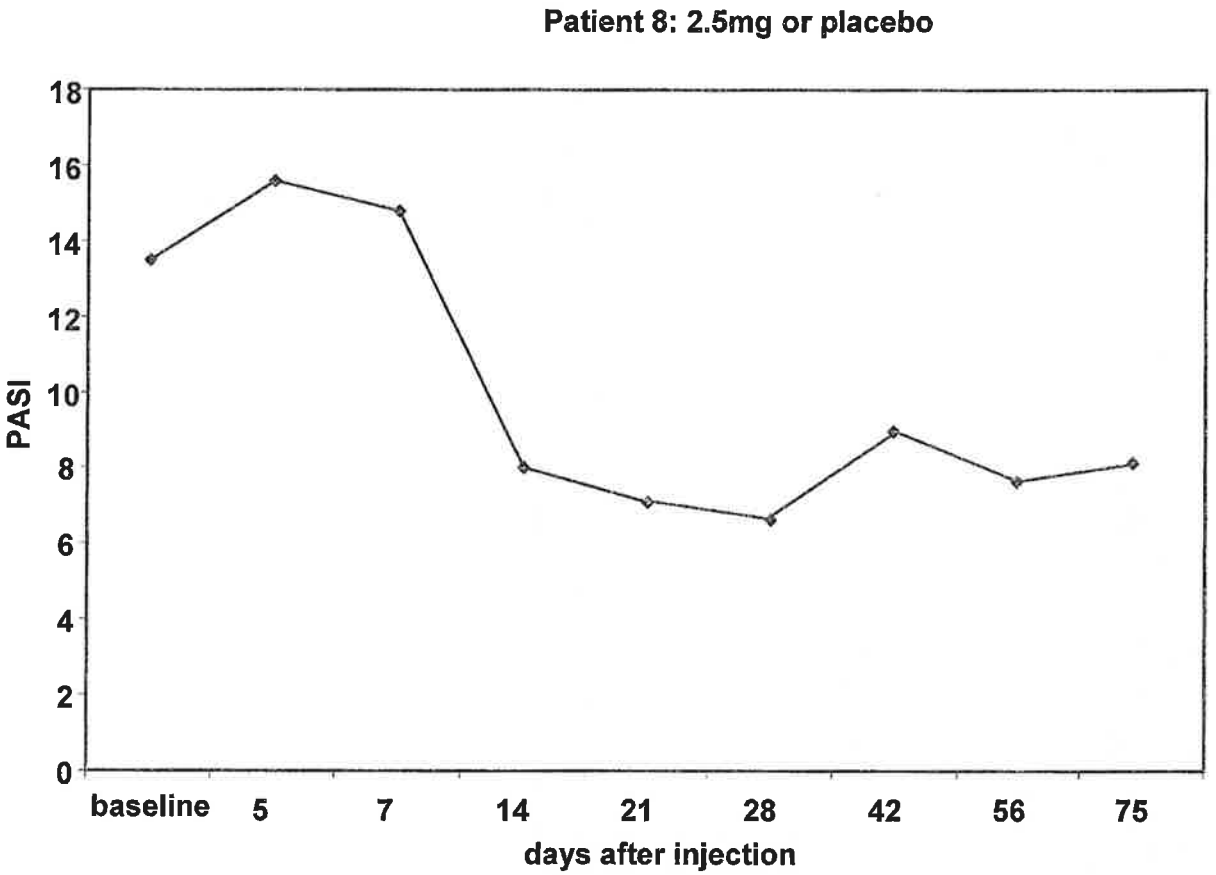

Patient 8: 2.5mg or placebo
PASI
18
16
14
12
10
8
6
4
2
0
baseline
5
7
14
21
28
42
56
75
days after injection

FIGURE 13H

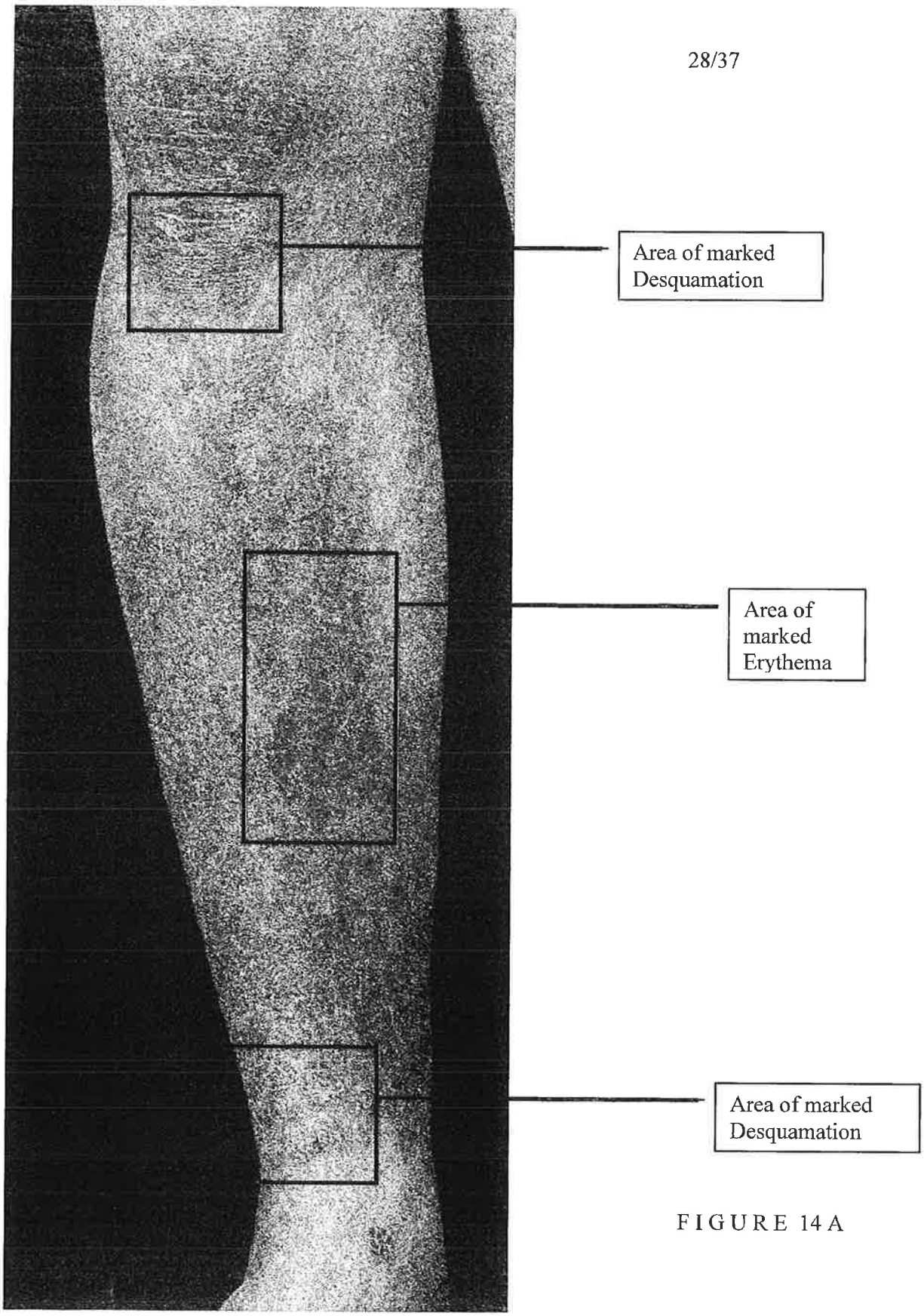

Area of marked Desquamation
Area of marked Erythema
Area of marked Desquamation

FIGURE 14A

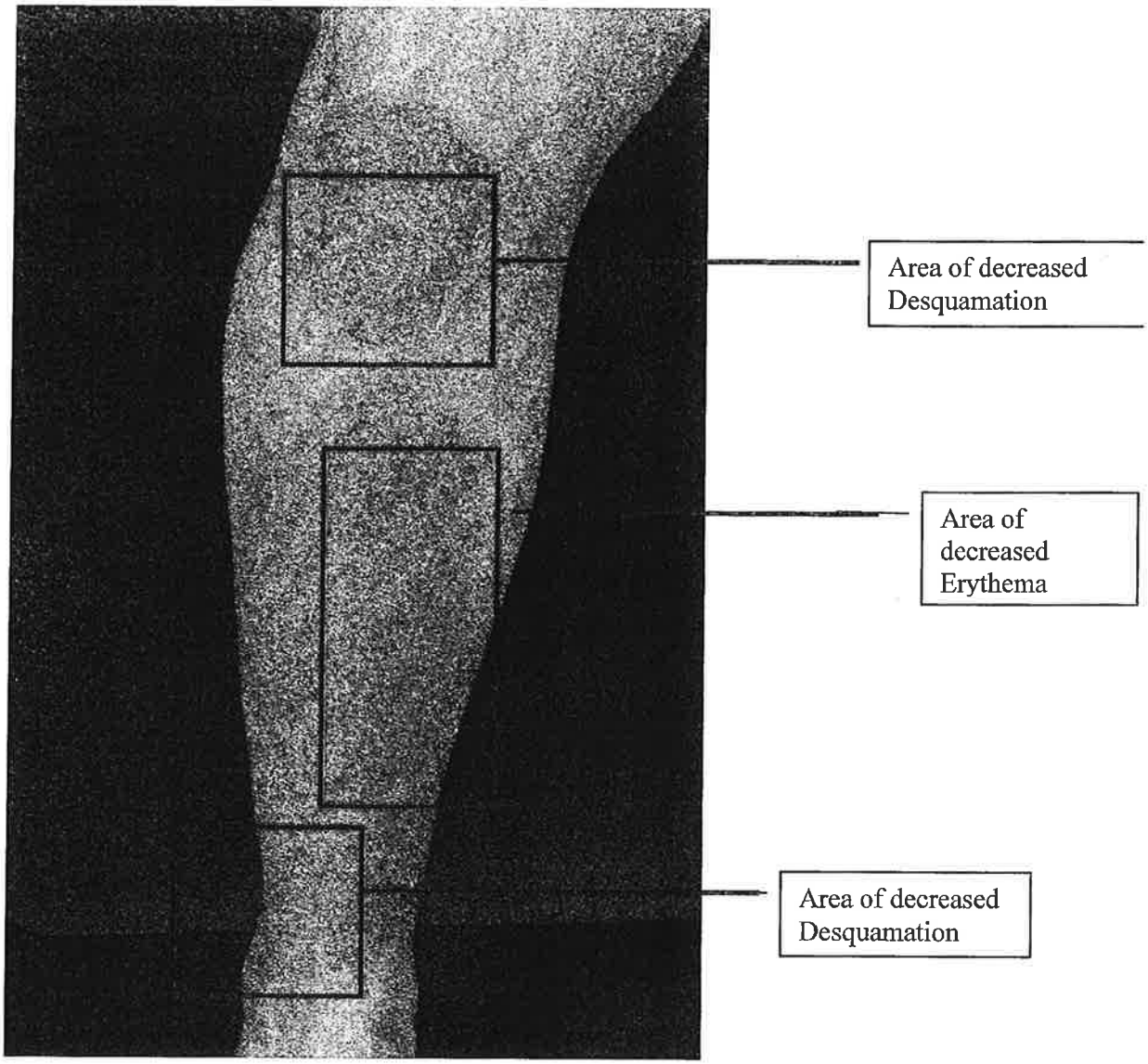

Area of decreased Desquamation
Area of decreased Erythema
Area of decreased Desquamation

FIGURE 14B

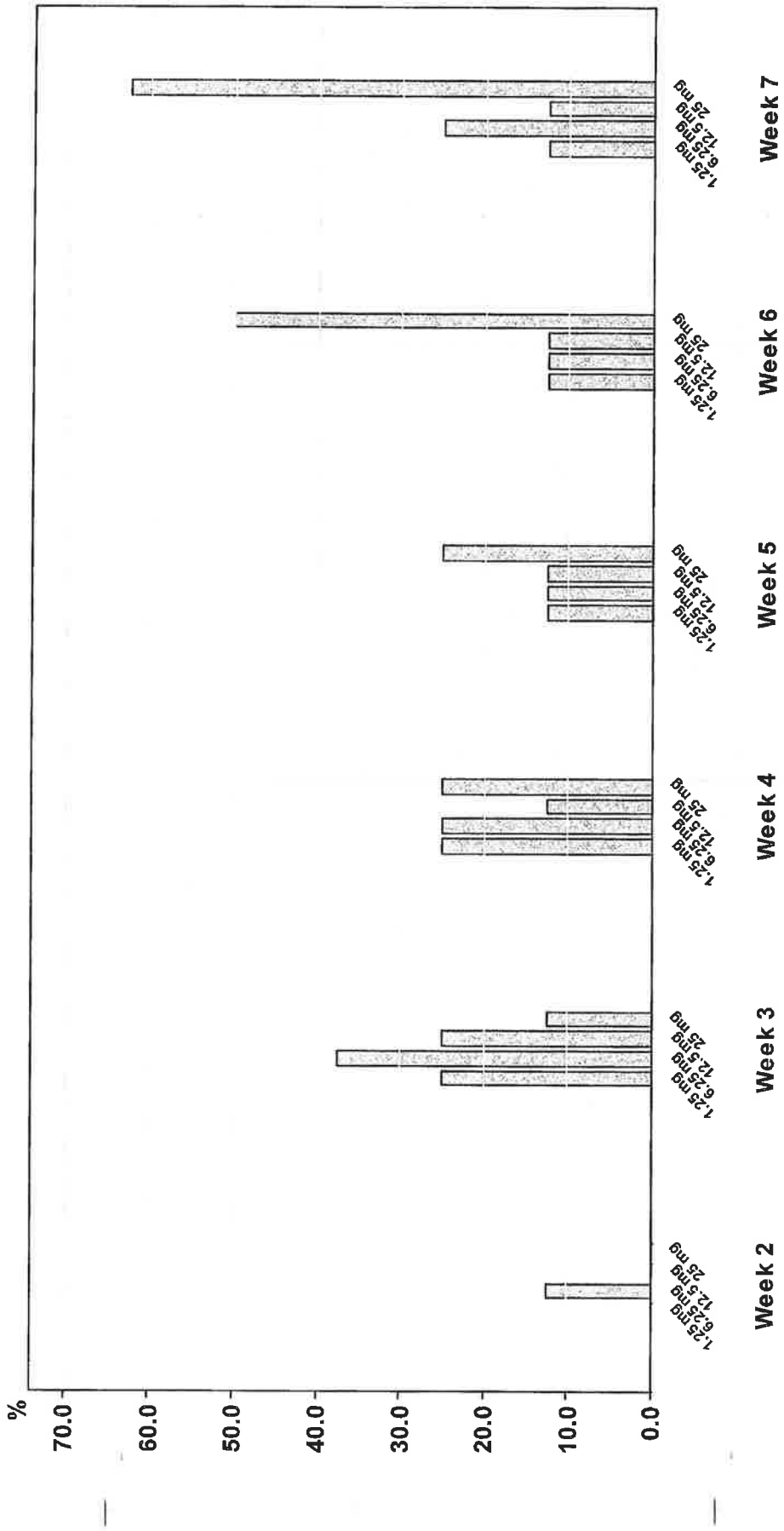

%
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
1.25 mg
6.25 mg
12.5 mg
25 mg
Week 2
Week 3
Week 4
Week 5
Week 6
Week 7

FIGURE 15

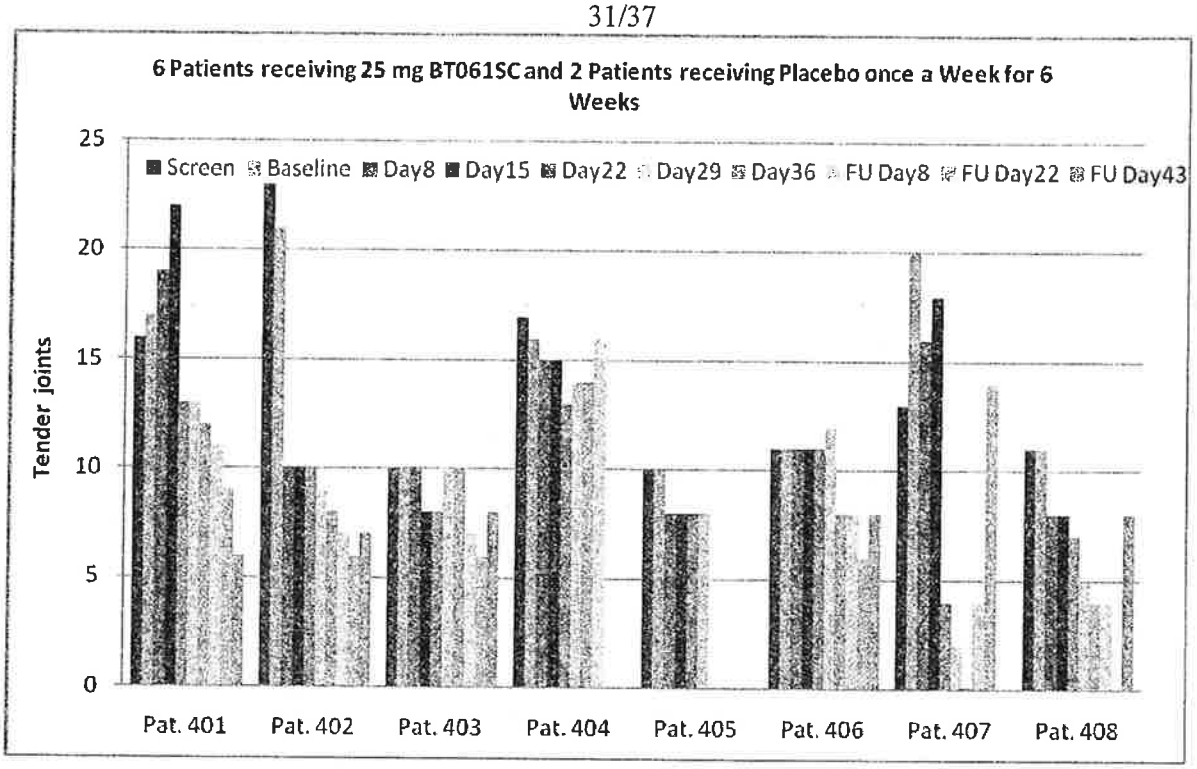


FIGURE 16A

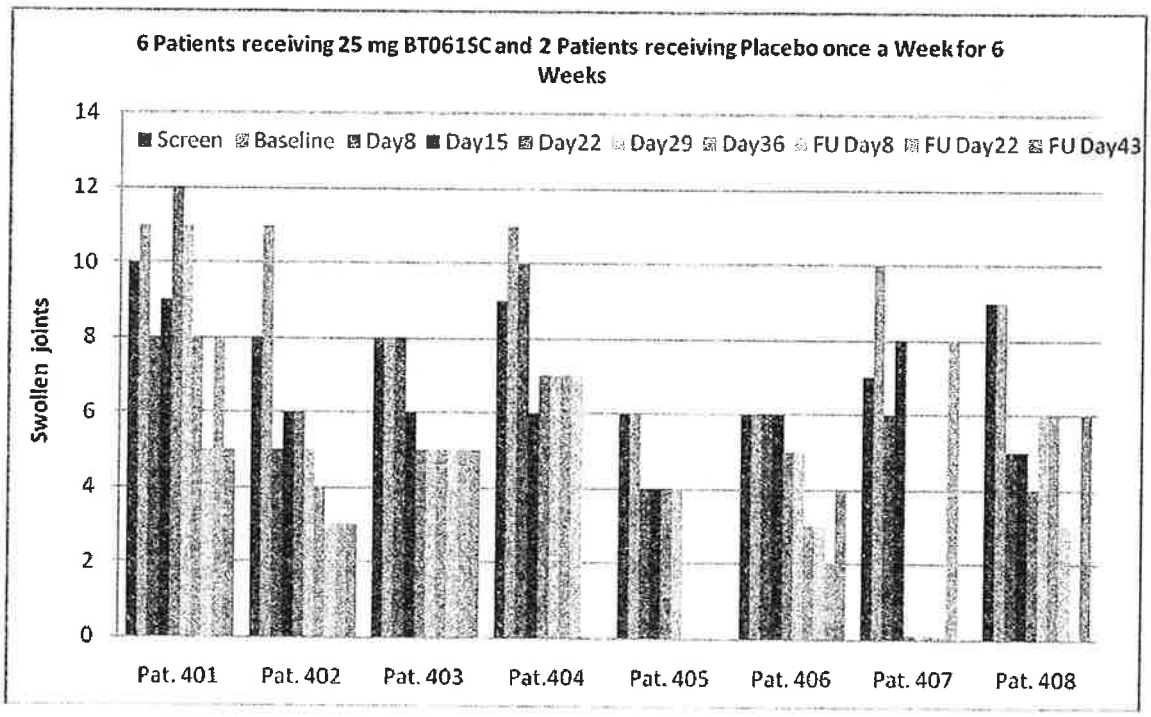


FIGURE 16B

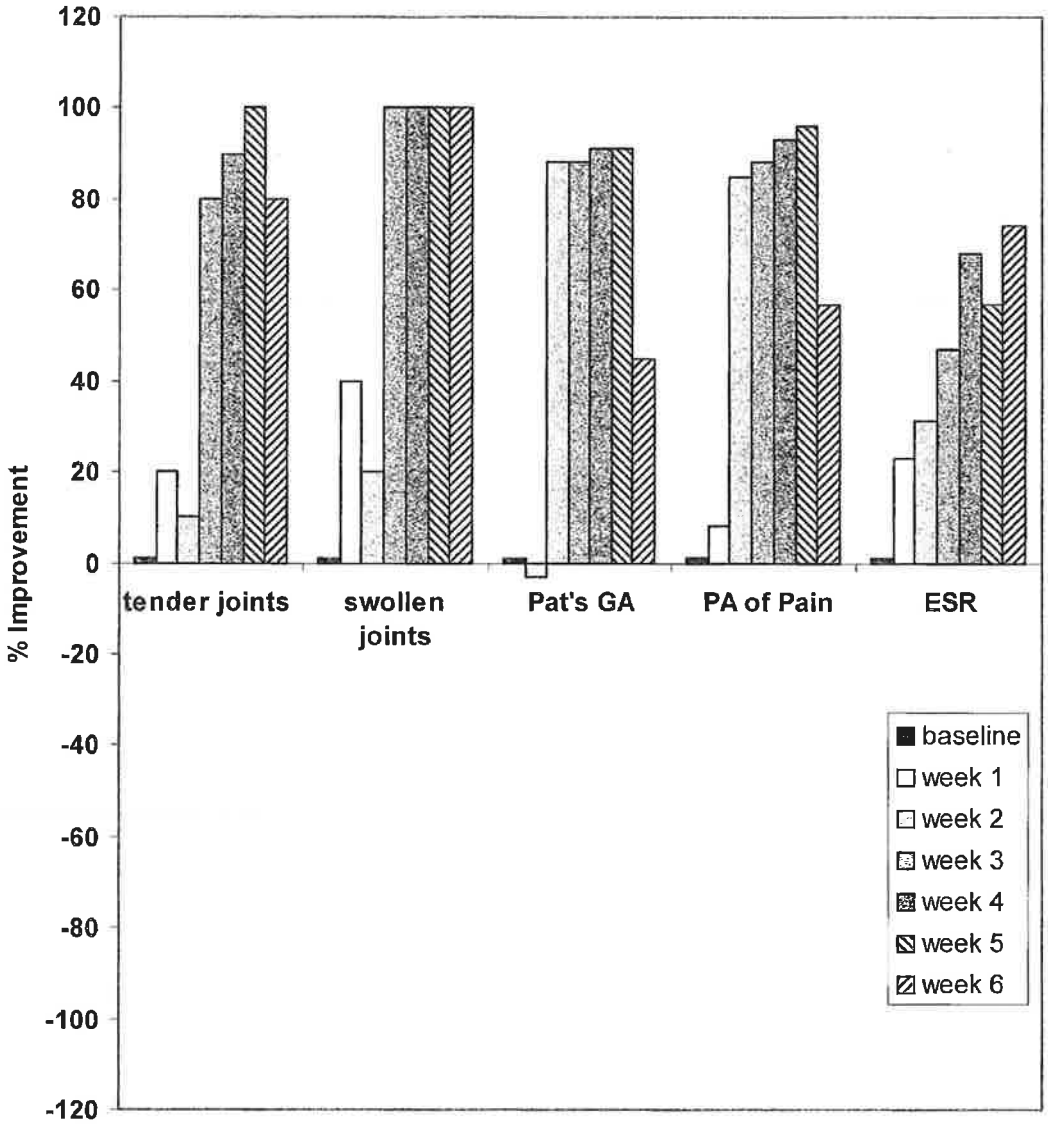

120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
% Improvement
tender joints
swollen joints
Pat's GA
PA of Pain
ESR
baseline
week 1
week 2
week 3
week 4
week 5
week 6

FIGURE 17A

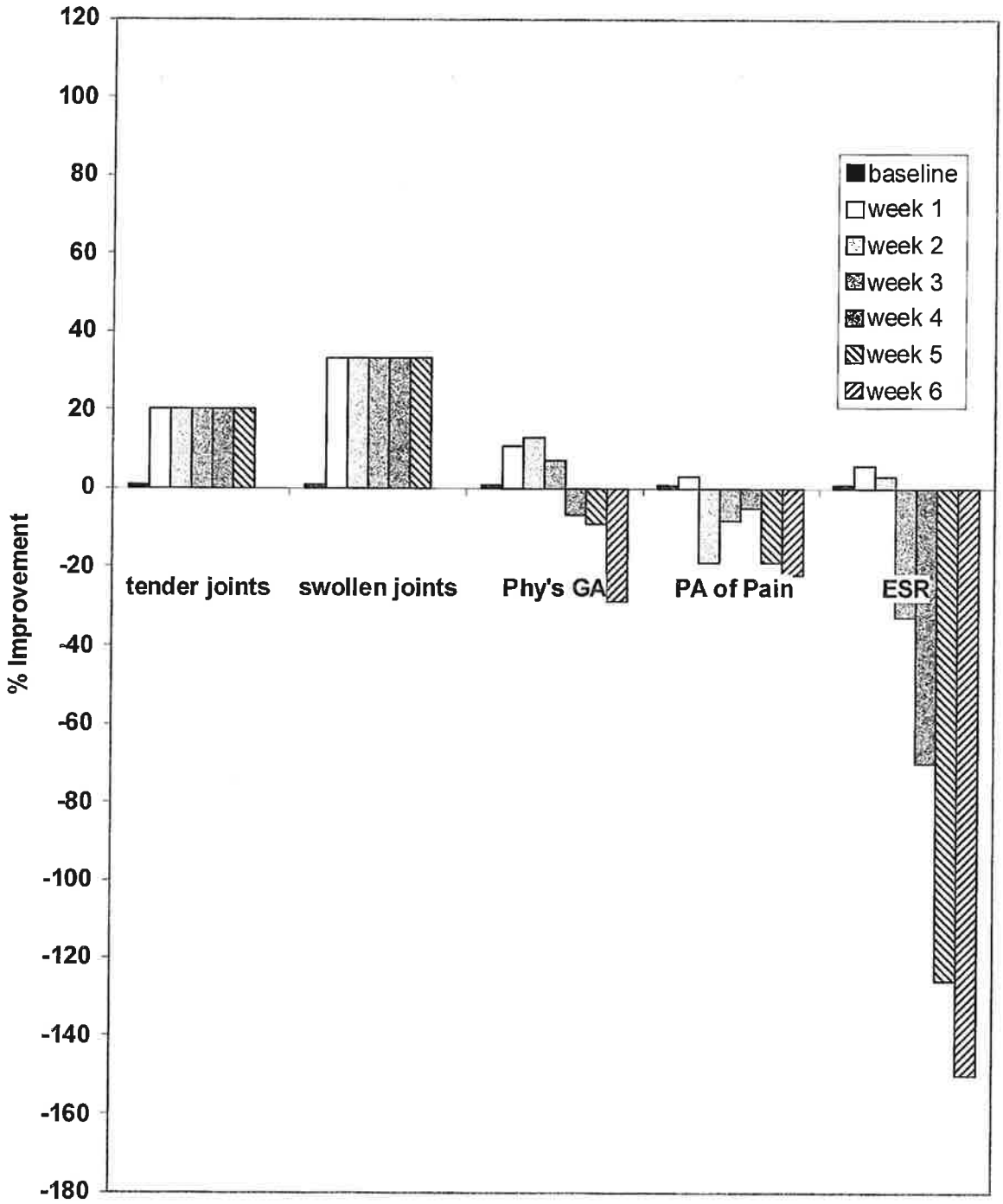

120
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
% Improvement
baseline
week 1
week 2
week 3
week 4
week 5
week 6
tender joints
swollen joints
Phy's GA
PA of Pain
ESR

FIGURE 17B

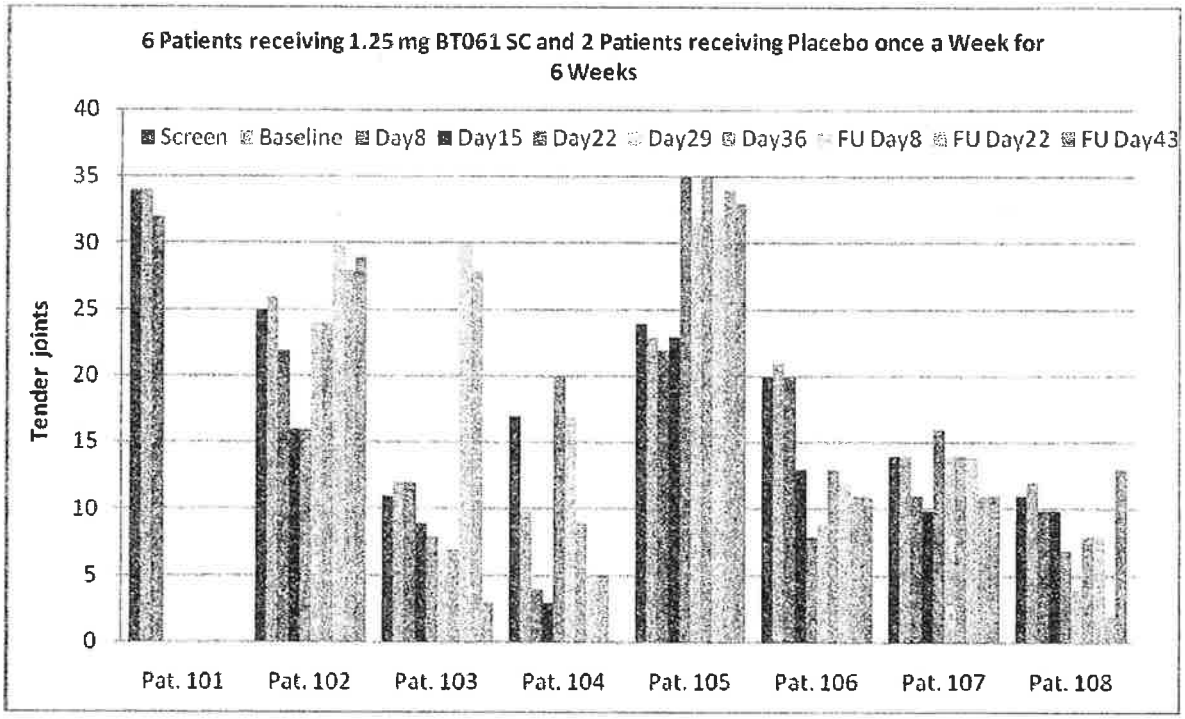


FIGURE 18A

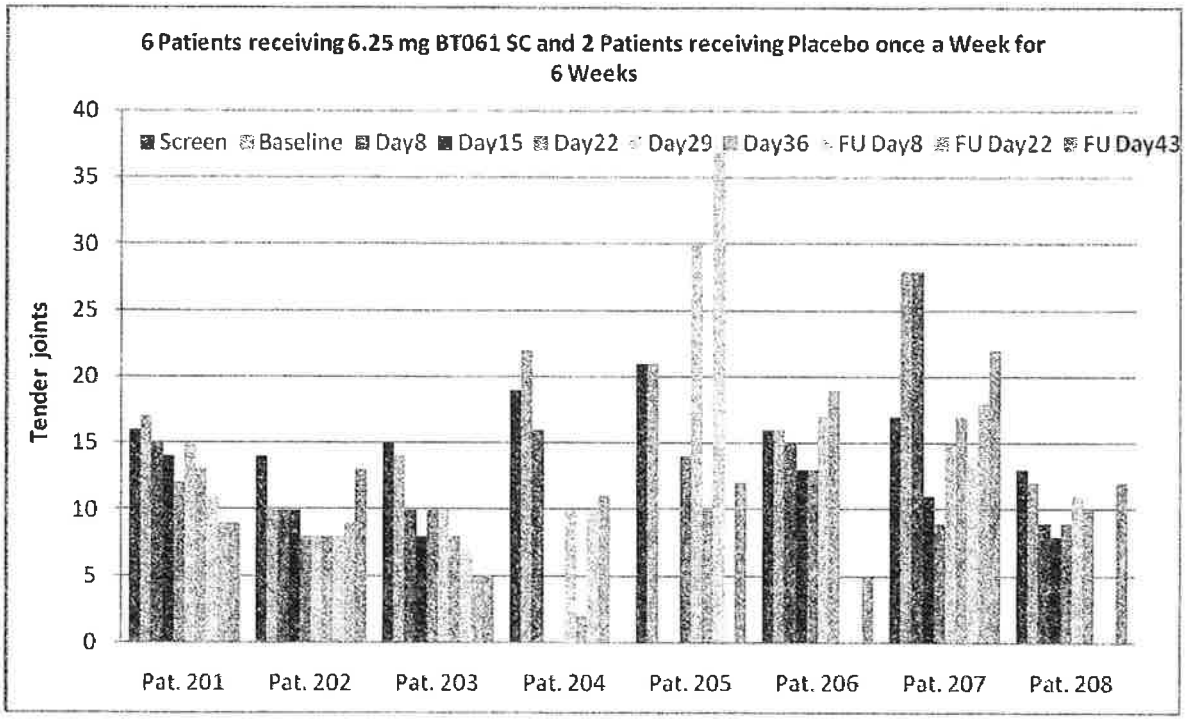


FIGURE 18B

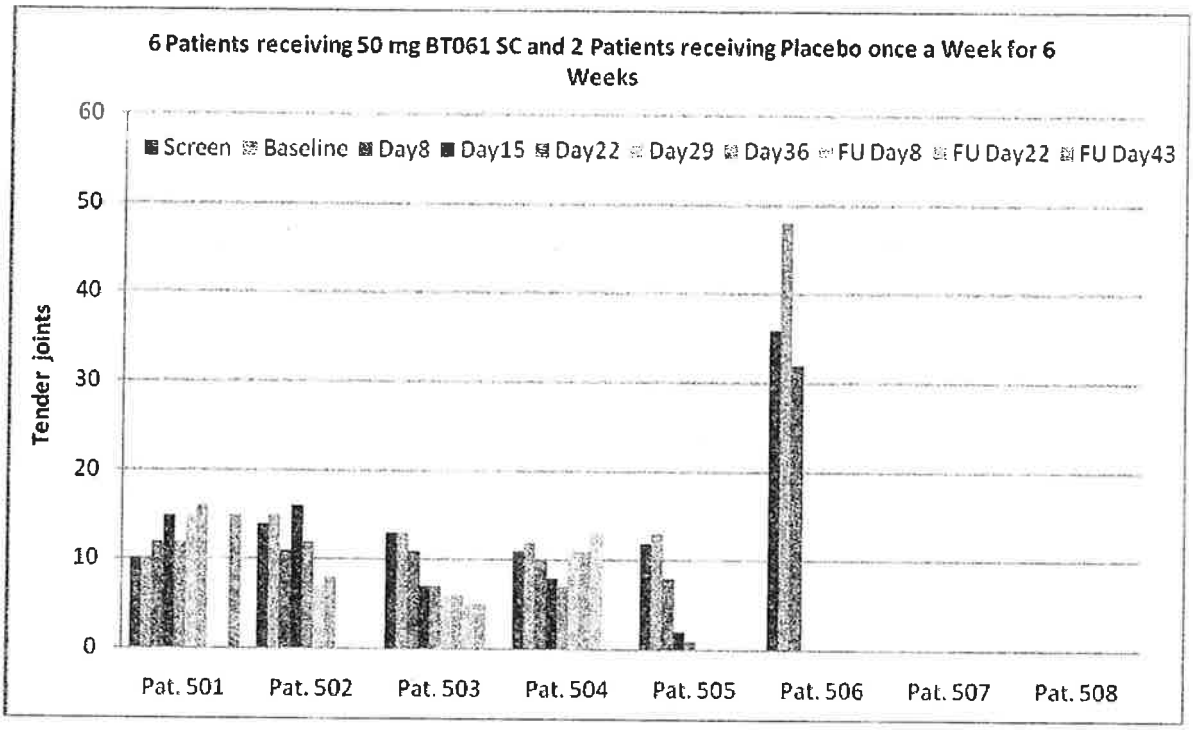


FIGURE 19A

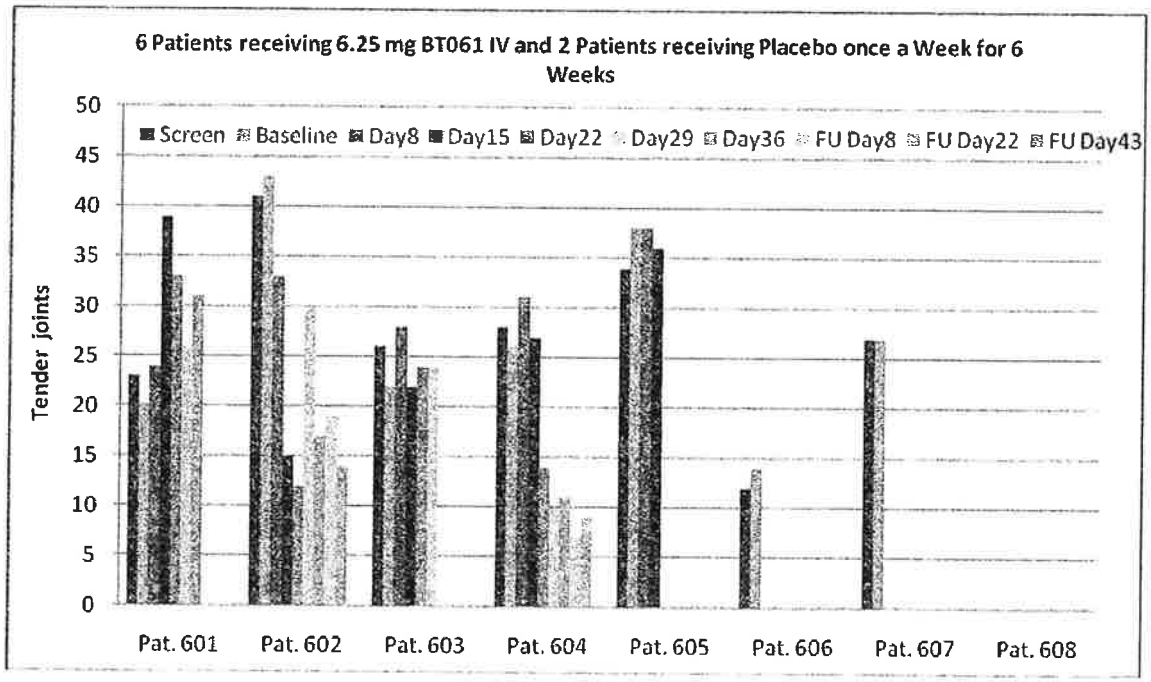


FIGURE 19B

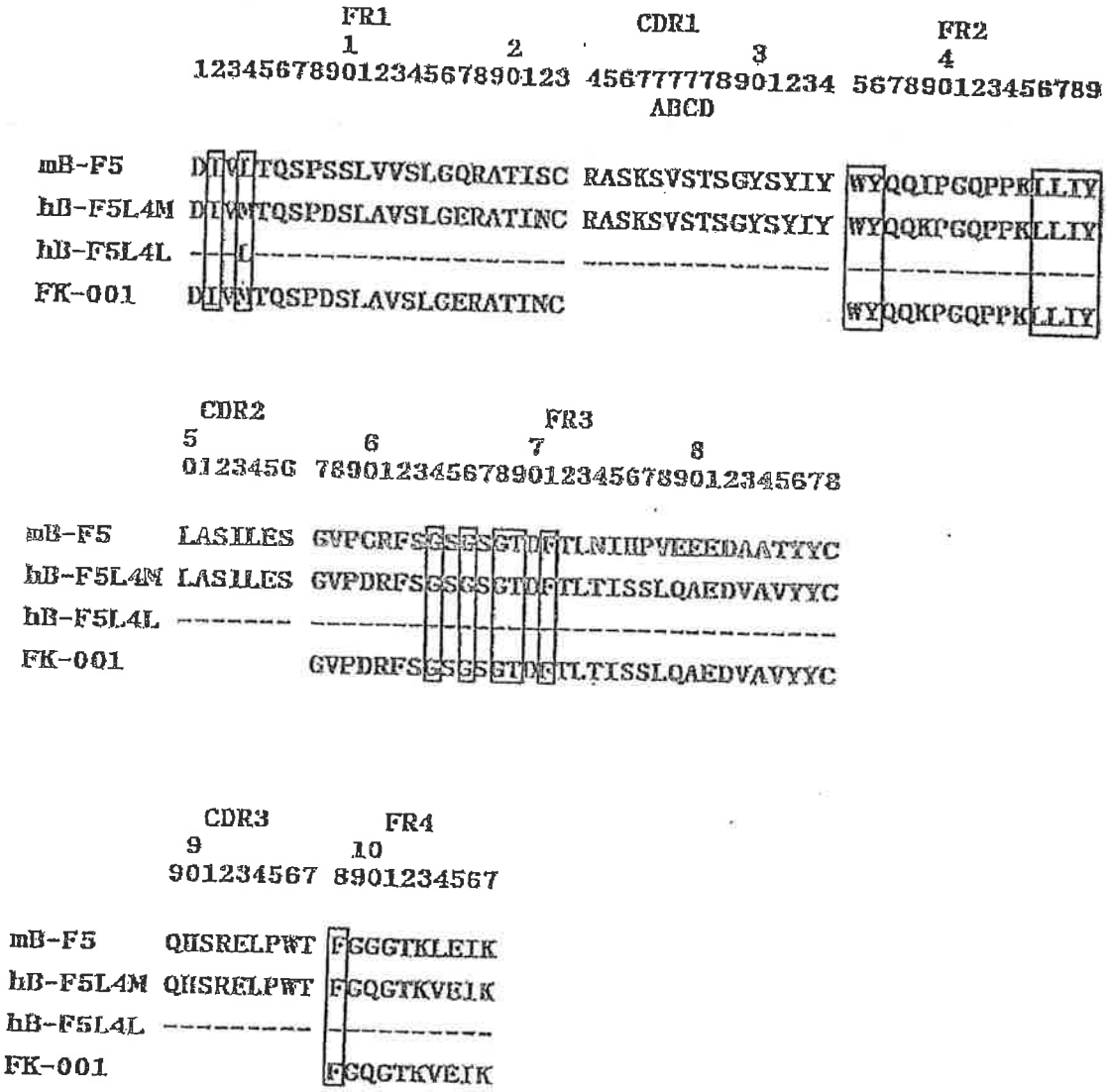

FR1
CDR1
FR2
1
2
3
4
12345678901234567890123 456777778901234 5678901234567 89
ABCD
mB-F5 DIVLTQSPSSLVVSLGQRATISC RASKSVSTSGYSYIY WYQQIPGQPPKLLIY
hB-F5L4M DIVMTQSPDSLAVSLGERATINC RASKSVSTSGYSYIY WYQQKPGQPPKLLIY
hB-F5L4L ---L---------- ---------- ----------
FK-001 DIVMTQSPDSLAVSLGERATINC WYQQKPGQPPKLLIY
CDR2
FR3
5
6
7
8
0123456 78901234567890123456789012345678
mB-F5 LASILES GVPGRFSGSGSGTDFTLNIHPVEEEDAATYYC
hB-F5L4M LASILES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC
hB-F5L4L ------- ----------
FK-001 GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC
CDR3
FR4
9
10
901234567 8901234567
mB-F5 QHSRELPWT FGGGTKLEIK
hB-F5L4M QHSRELPWT FGQGTKVEIK
hB-F5L4L --------- ----------
FK-001 FGQGTKVEIK

FIGURE 20

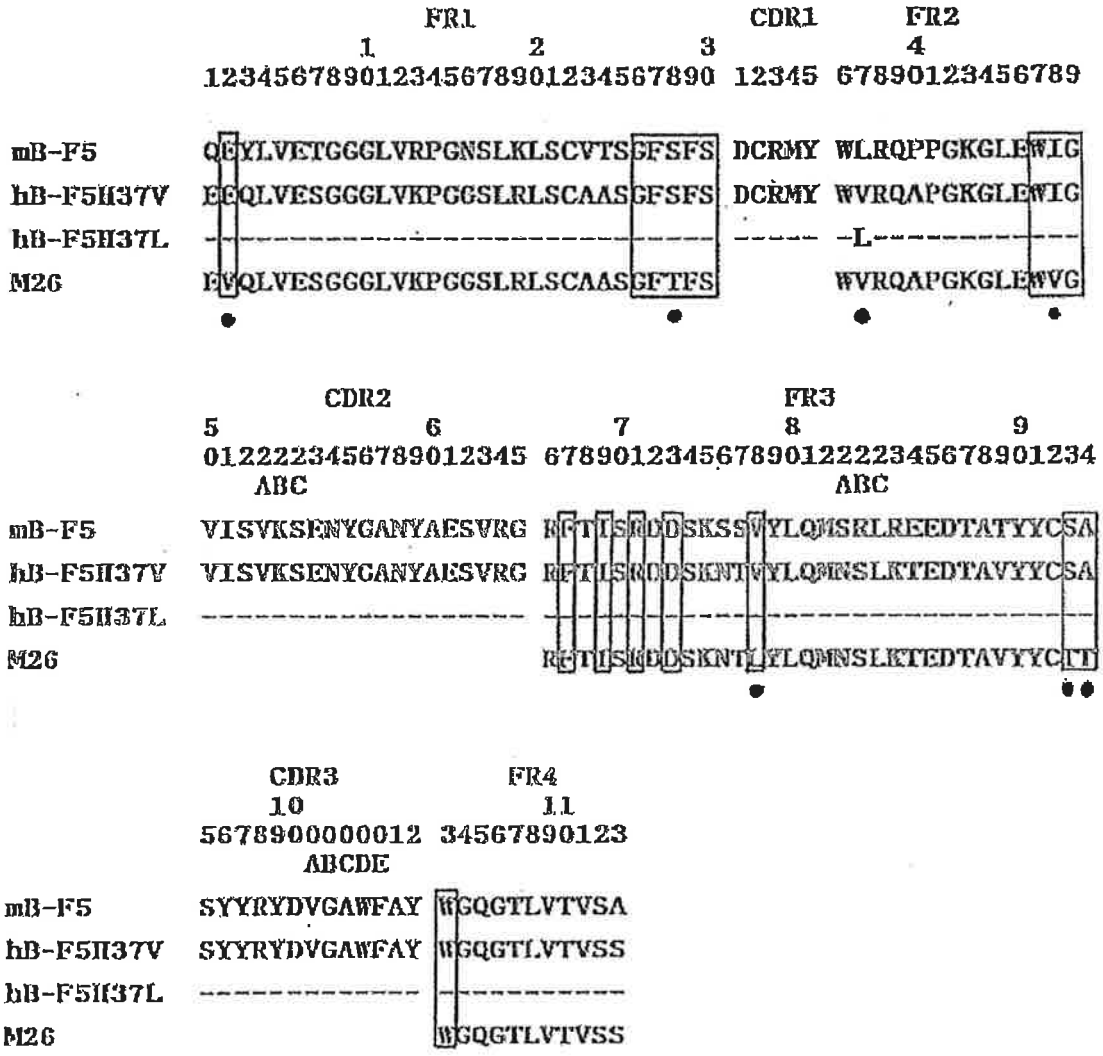

FR1
CDR1
FR2
1
2
3
4
12345678901234567890123456789012345 67890123456789
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hB-F5H37V EEQLVESGGGLVKPGGSLRLSCAASGFSFS DCRMY WVRQAPGKGLEWIG
hB-F5H37L ---------- ----- -L----------
M26 EVQLVESGGGLVKPGGSLRLSCAASGFTFS WVRQAPGKGLEWVG
CDR2
FR3
5
6
7
8
9
012222345678901234567890123456789012222345678901234
ABC
ABC
mB-F5 VISVKSENYGANYAESVRG RFTISRDDSKSSVYLQMSRLREEDTATYYCSA
hB-F5H37V VISVKSENYGANYAESVRG RFTISRDDSKNTVYLQMNSLKTEDTAVYYCSA
hB-F5H37L ---------- ----------
M26 RFTISRDDSKNTLYLQMNSLKTEDTAVYYCTT
CDR3
FR4
10
11
5678900000012 34567890123
ABCDE
mB-F5 SYYRYDVGAWFAY WGQGTLVTVSA
hB-F5H37V SYYRYDVGAWFAY WGQGTLVTVSS
hB-F5H37L ---------- ----------
M26 WGQGTLVTVSS

FIGURE 21