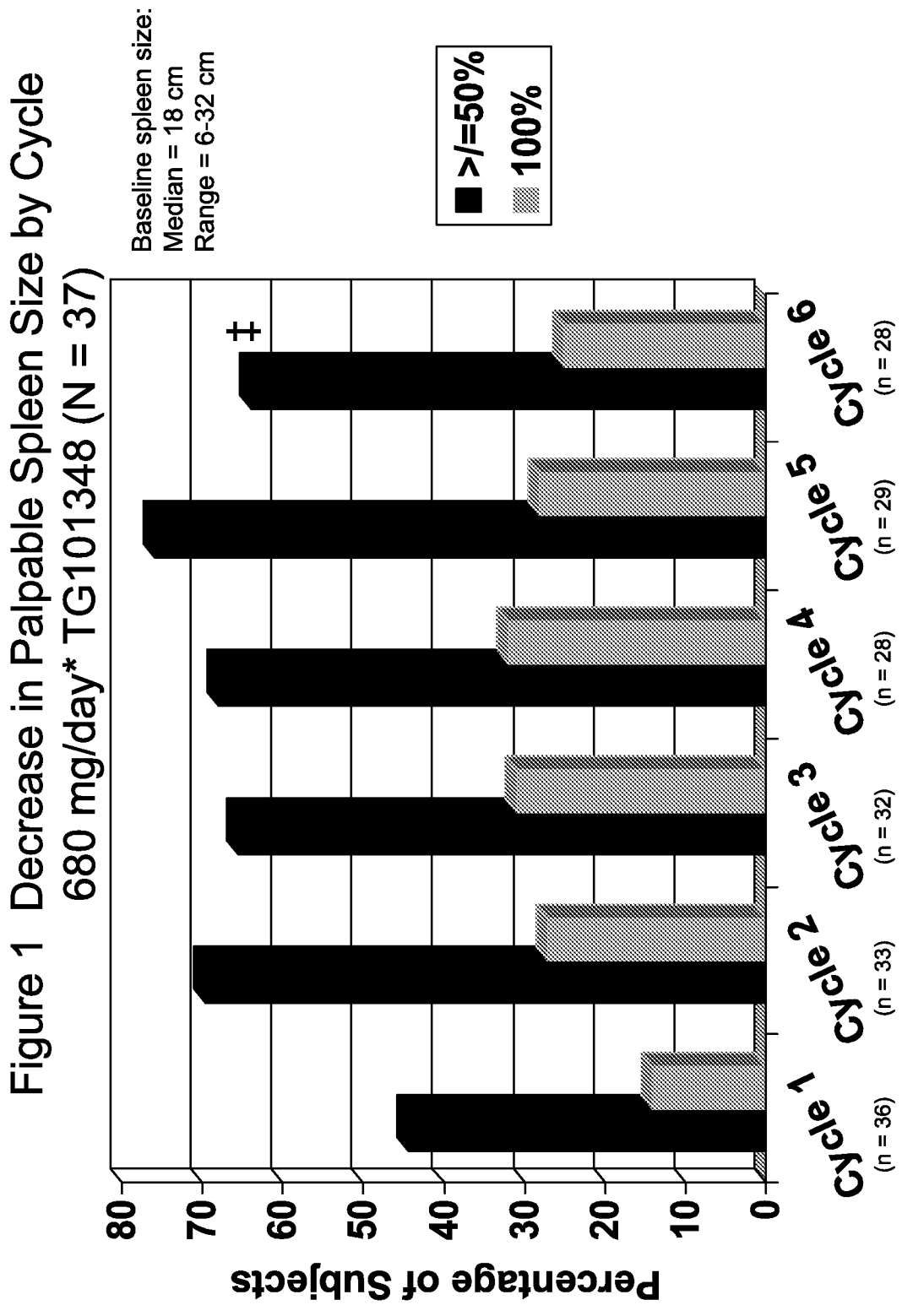
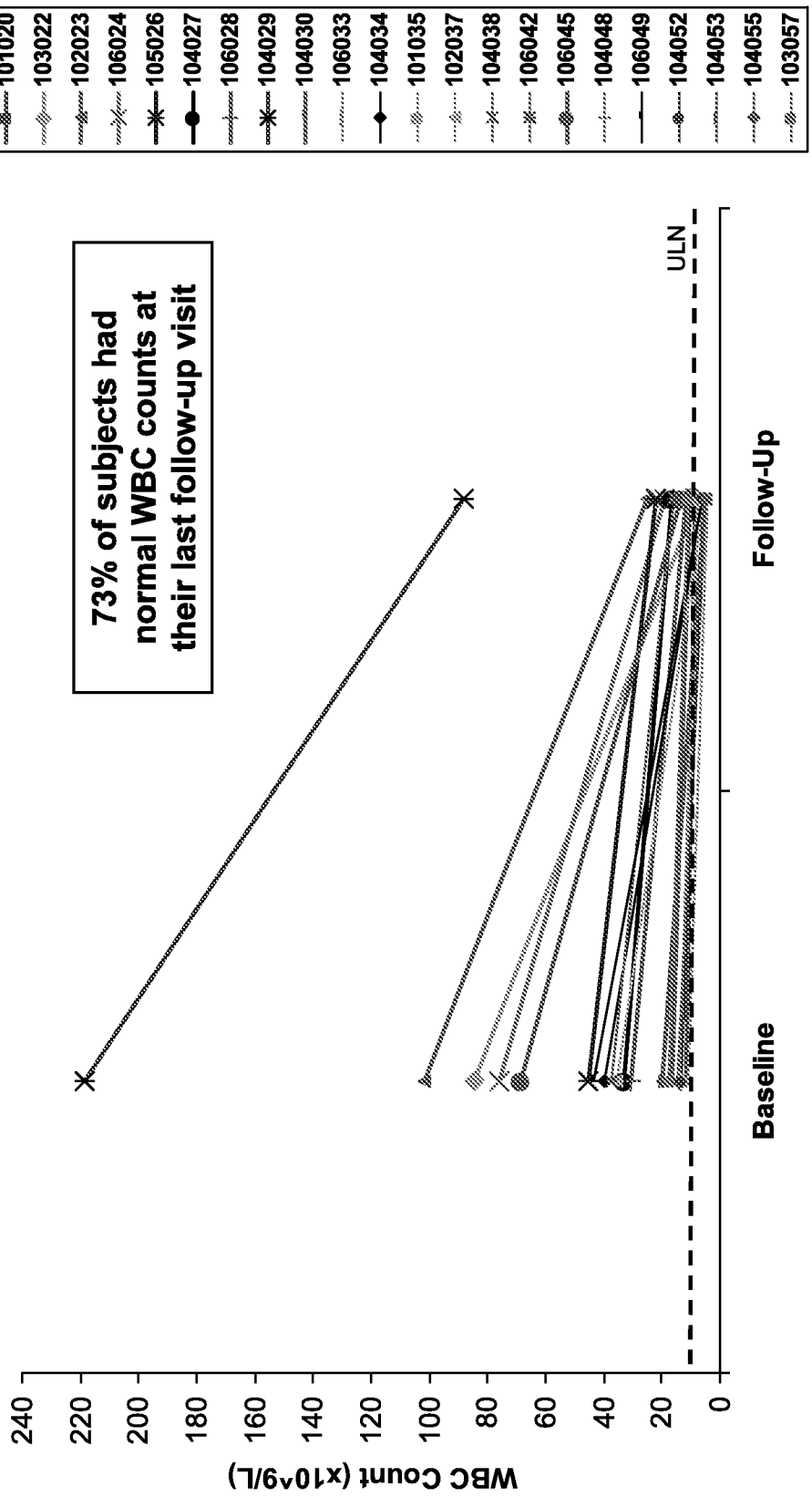


*Starting dose. Doses (mg/day) Cycle 1, 520-800; Cycles 2-6, 360-680 mg/day.
‡22-47% increase in 3 subjects with drug held for ~2-3 weeks immediately prior to measurement.

Figure 2 TG101348 Effect on Leukocytosis (Baseline WBC Count > 11 x 10^9/L)



Doses at follow-up range from 360 to 680 mg/day. Last follow-up visit ranges from 8 to 24 weeks (median 24 weeks).
ULN = upper limit of normal.

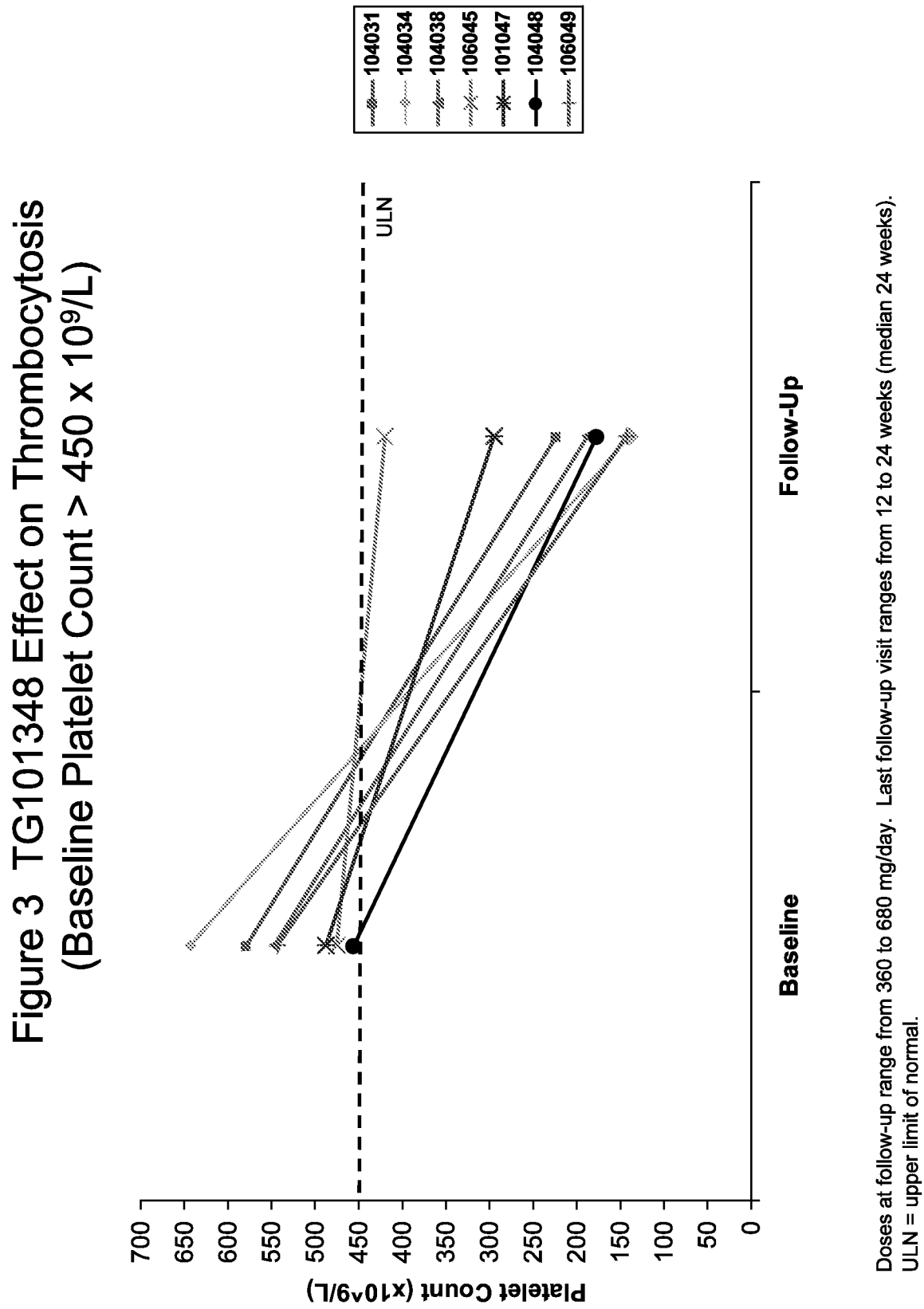
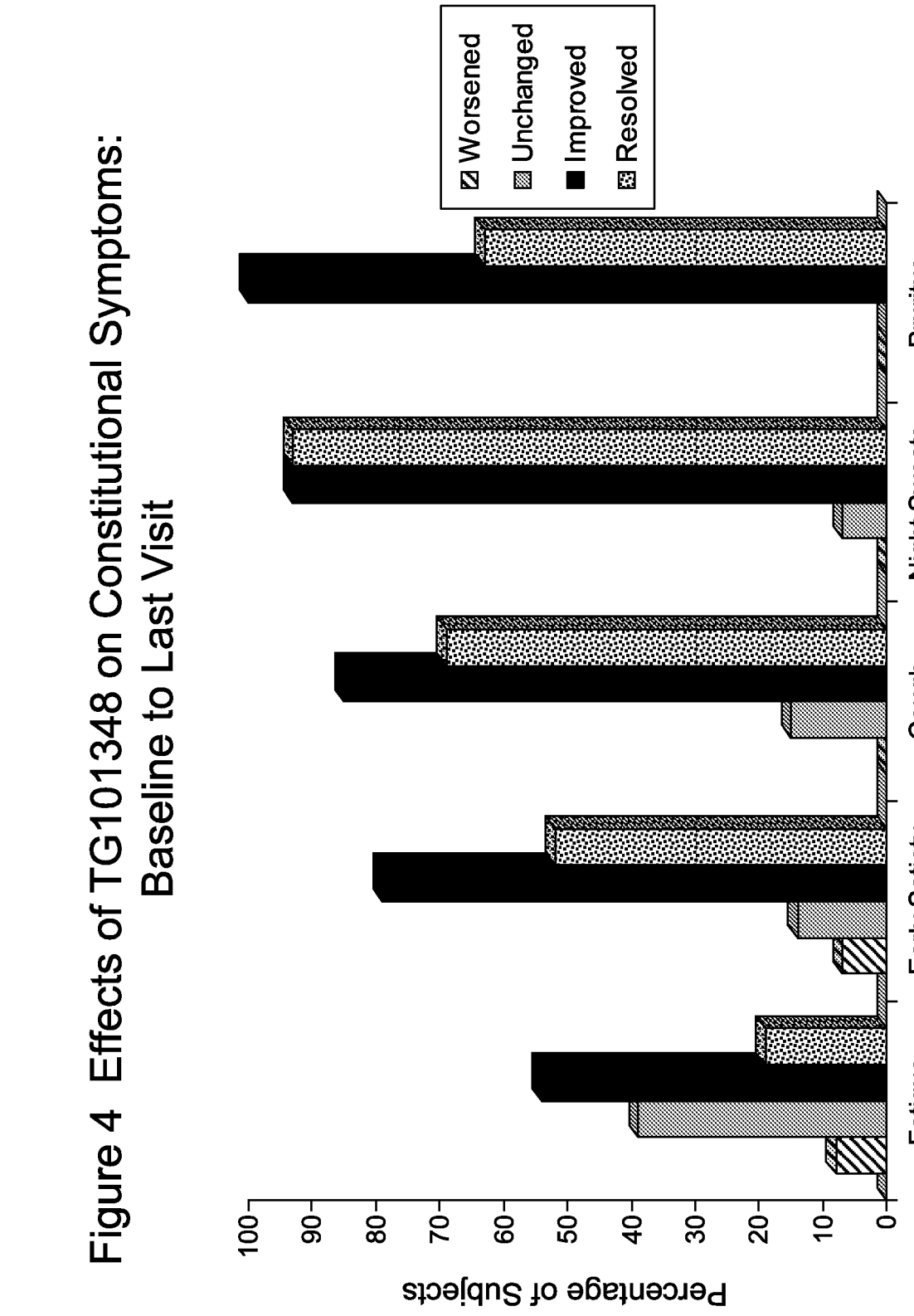


Figure 3 TG101348 Effect on Thrombocytosis (Baseline Platelet Count > 450 x 10^9/L)

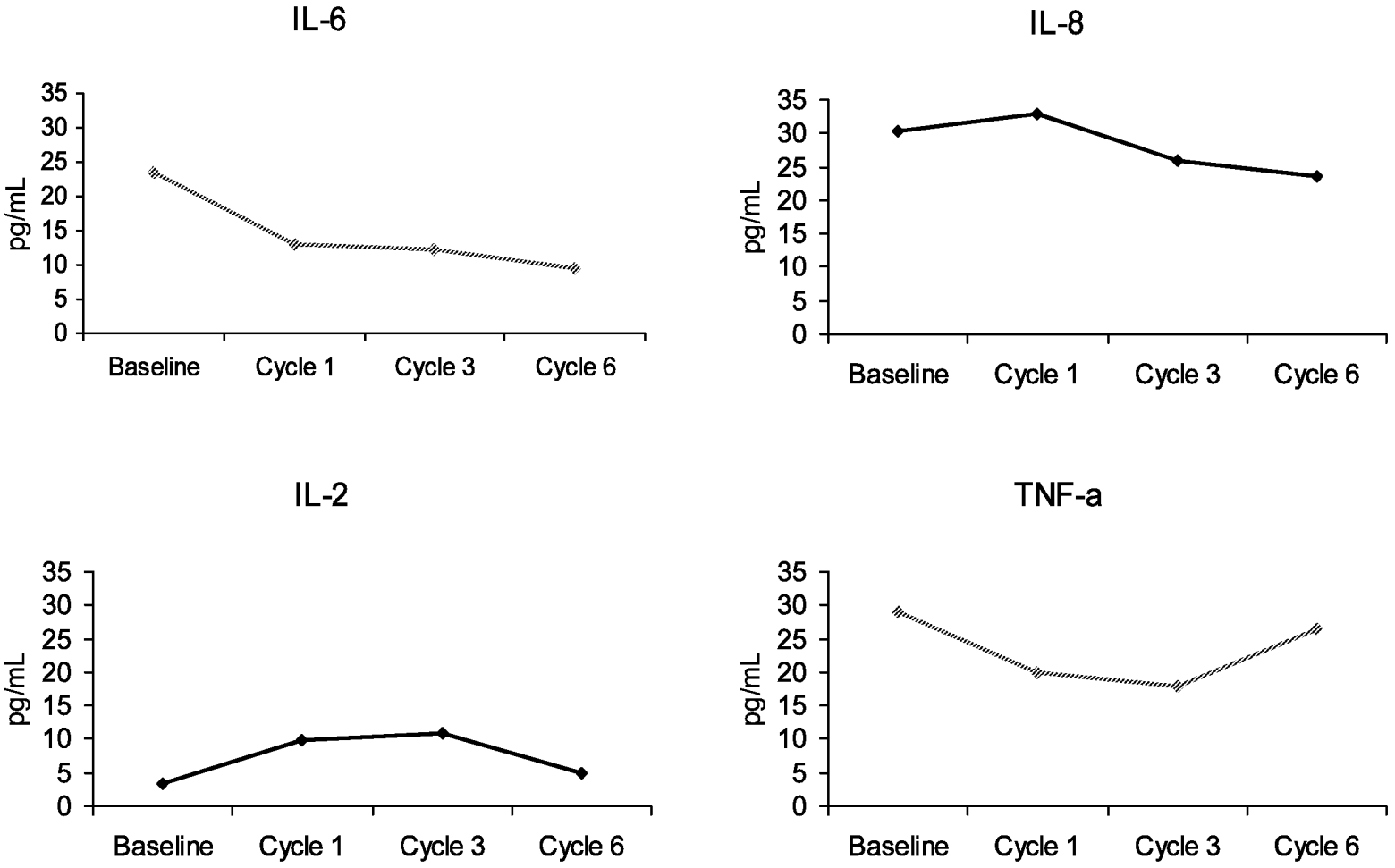
Doses at follow-up range from 360 to 680 mg/day. Last follow-up visit ranges from 12 to 24 weeks (median 24 weeks).
ULN = upper limit of normal.

Figure 4 Effects of TG101348 on Constitutional Symptoms: Baseline to Last Visit



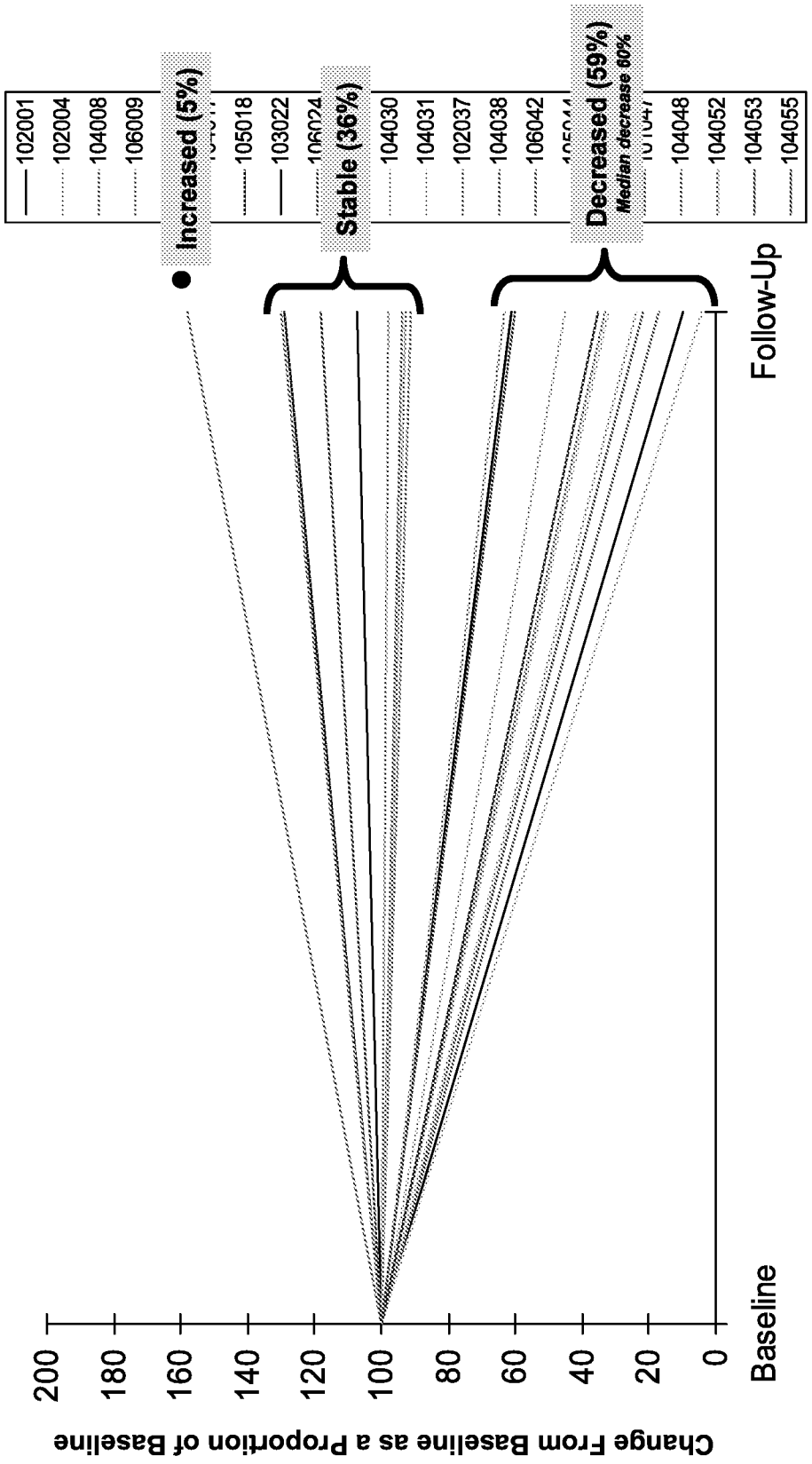
Last visit ranges from 4 to 24 weeks (median 20 weeks). Data reflect changes from symptoms present at baseline. 18 subjects reported new onset of ≥ 1 symptom during the study; of these, symptoms for 12 subjects were resolved by last follow-up visit.
Severity rated by subjects on scale of 1-10. For analysis, 0 = absent; 1-3 = mild; 4-7 = moderate; 8-10 = severe. Improved = downgrade to absent or to mild or moderate from more severe rating at baseline.

Figure 5 No Significant Changes in Cytokine Levels With TG101348



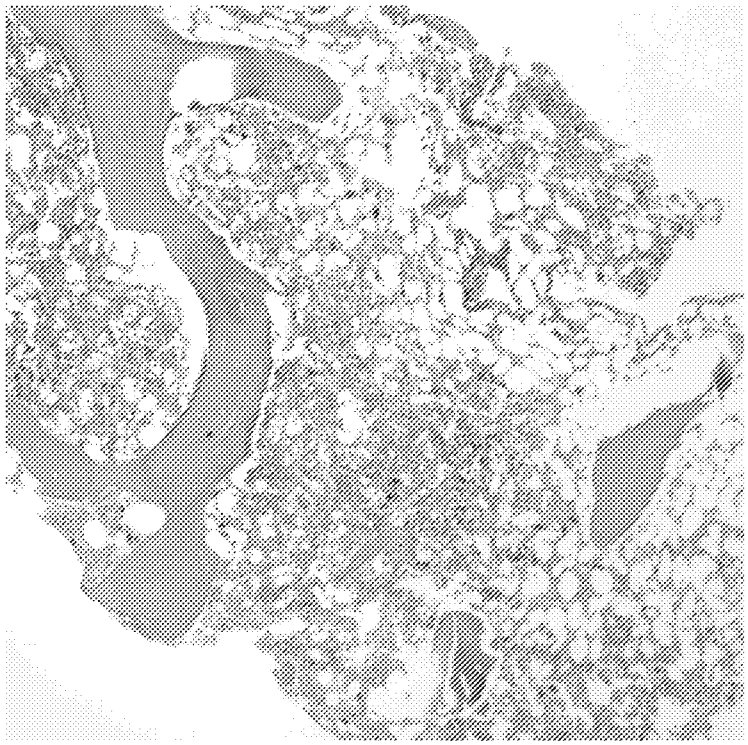
All values are medians.

Figure 6 TG101348 Effect on V617F Allele Burden in Subjects With Baseline > 20% (N = 22)*



*Subset of JAK2V617F positive subjects in the overall population (N = 48).
Doses at follow-up 360 to 680 mg/day. Last follow-up visit ranges from 20 to 72 weeks (median 24 weeks).

Figure 7 Effect on BM Cellularity



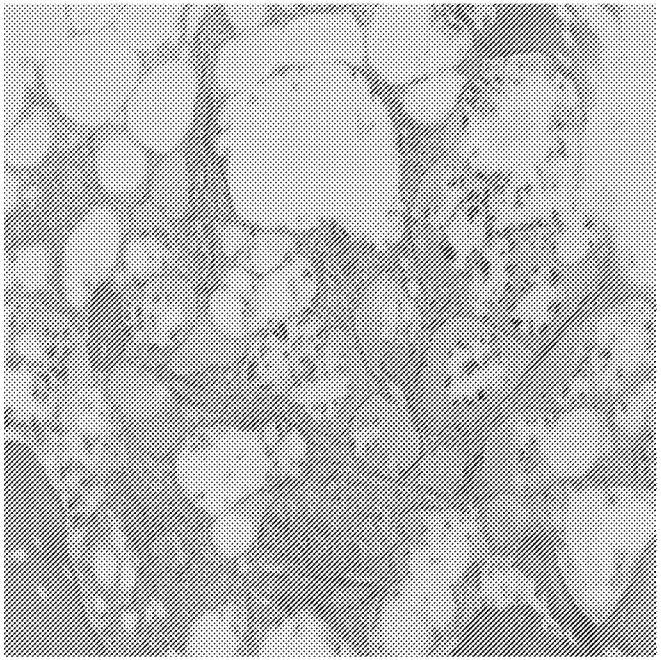
Baseline: 60% cellularity



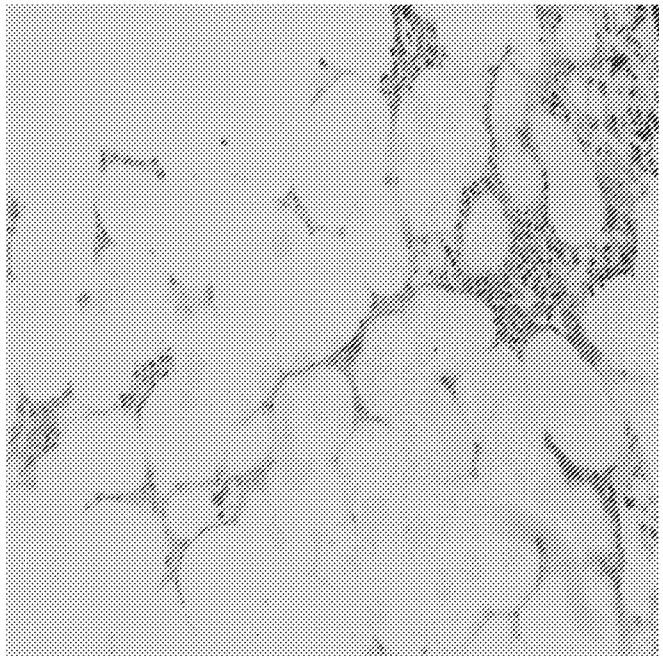
After 18 cycles: 5-10% cellularity

76-year-old male, V617F negative PMF; starting dose, 30 mg/day; dose at follow-up, 520 mg/day.

Figure 8 Effect on BM Fibrosis



Baseline: 3+

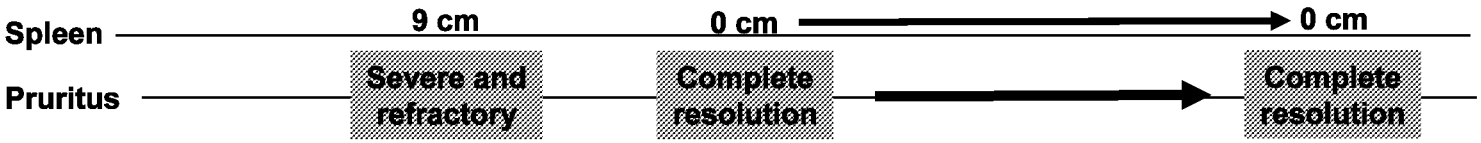


After 18 cycles: 0

56-year-old male, V617F negative PMF; starting dose, 240 mg/day; dose at follow-up, 440 mg/day.

Figure 9 A subject with JAK2V617F-positive PMF started at 680 mg/day (TG101348)

	Day -8	Screen -1	C1D8 *680mg*	C2D1 *680mg*	C2D15 *680mg*	C3D1 *360mg*	C6D1 *360mg*	C9D1 *360mg*
Hgb (g/dL)	9	9	9.4	7.9**	9.2	8	9.6	10.9
WBC (x 109/L)	13.5	14.9	18.6	7.1	6.2	7.3	5.4	5.2
Meta	2	0	n/a	0	0	0	0	0
Myelo	10	6		0	0	0	0	1
Blasts	0	1		0	1	0	0	0
nuRBC	18	10		0	0	0	1	0
Plt (x 109/L)	577	546	731	289	183	183	192	212
LDH U/L	943	928	1001	581	529	479	455	444



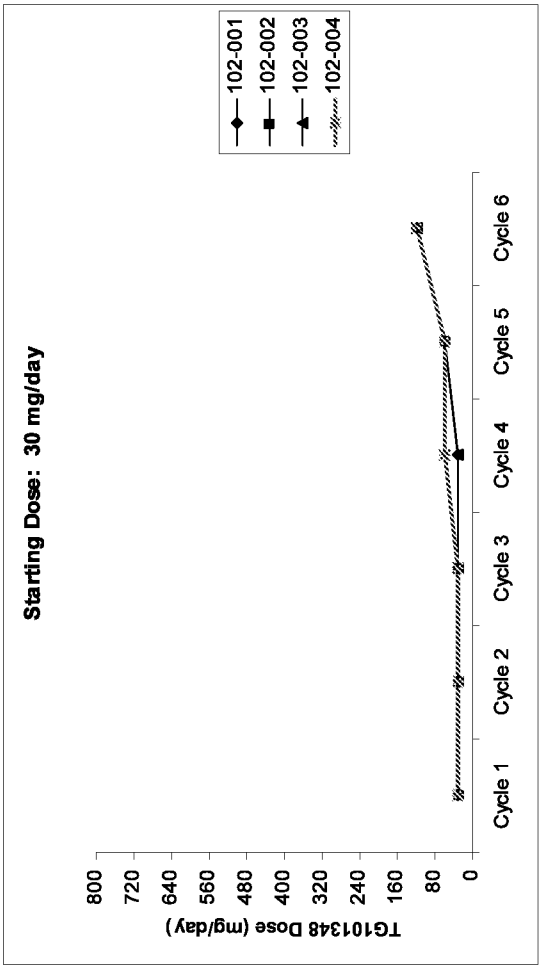


Figure 10A

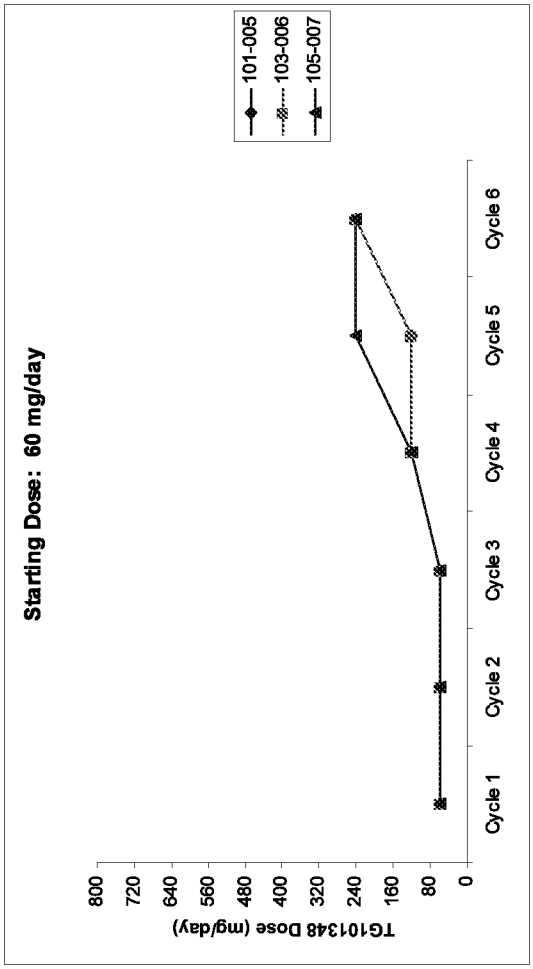


Figure 10B

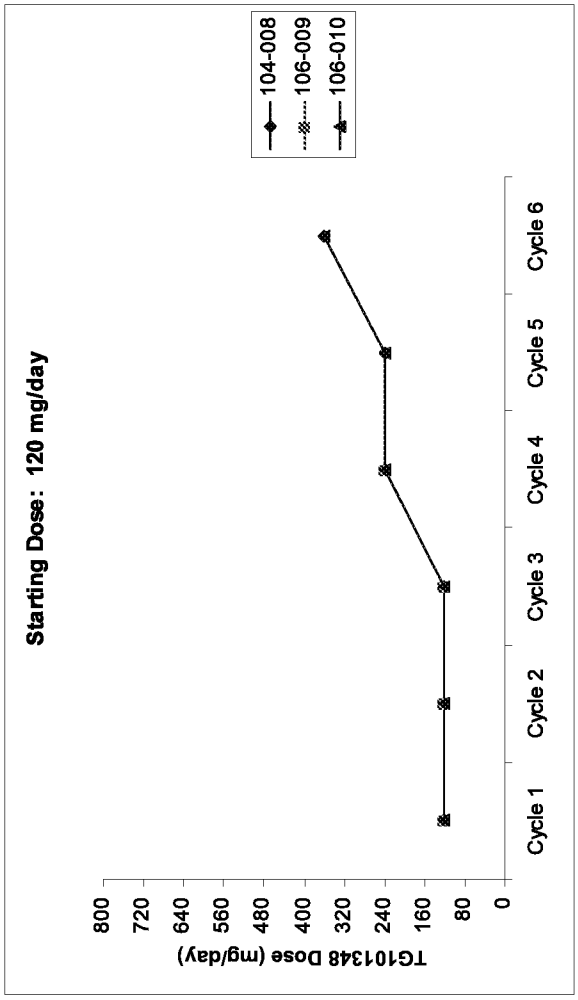


Figure 10C

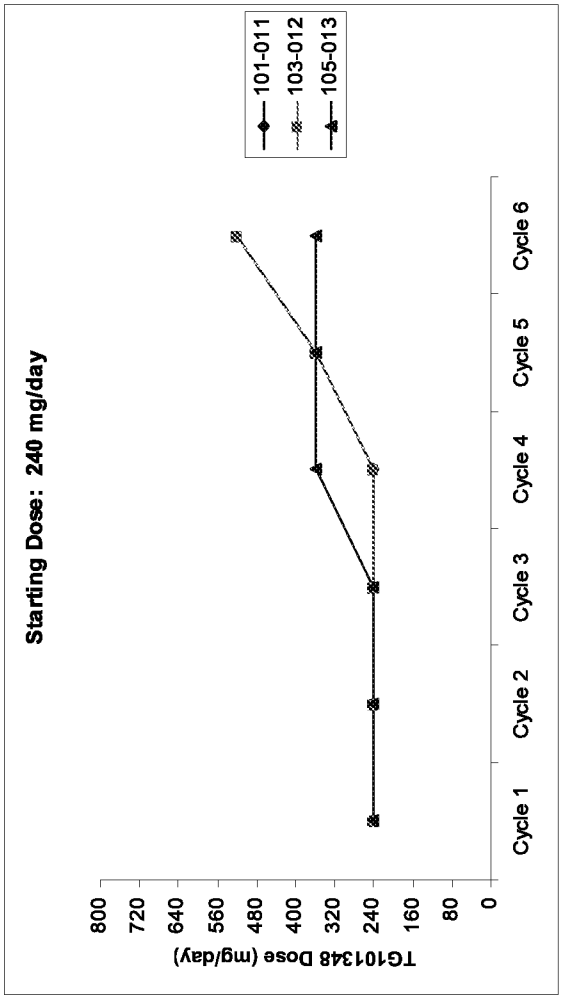


Figure 10D

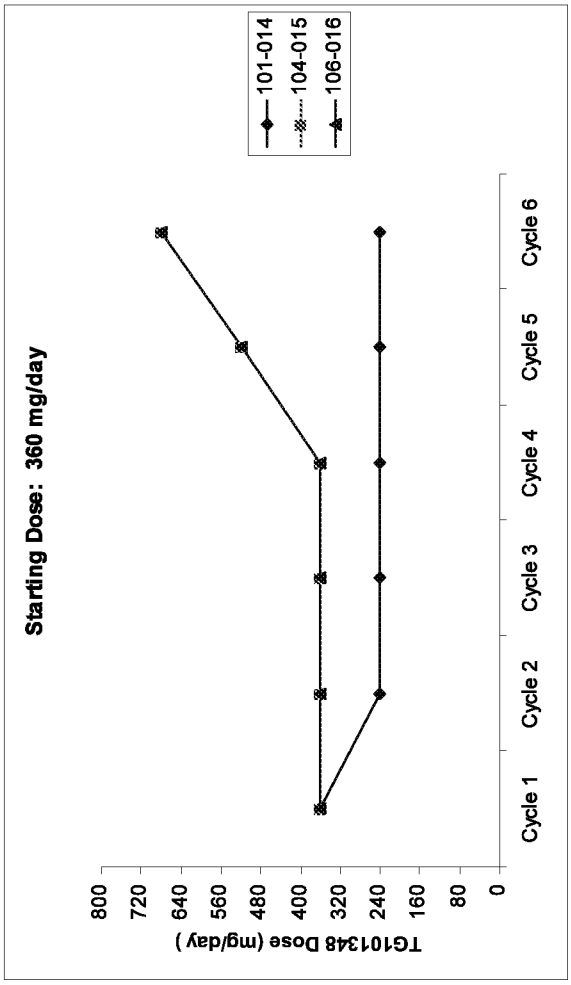


Figure 10E

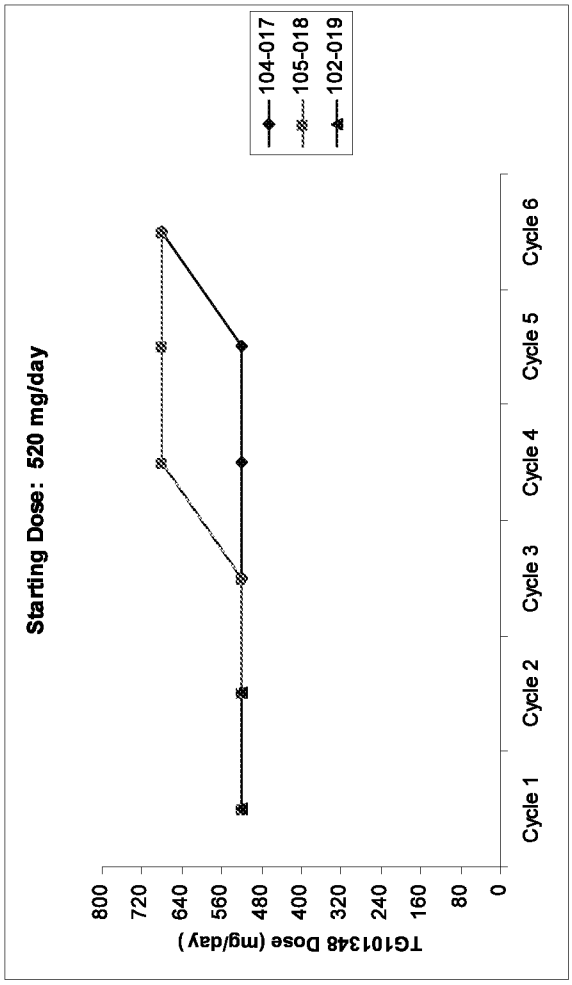


Figure 10F

Figure 10G

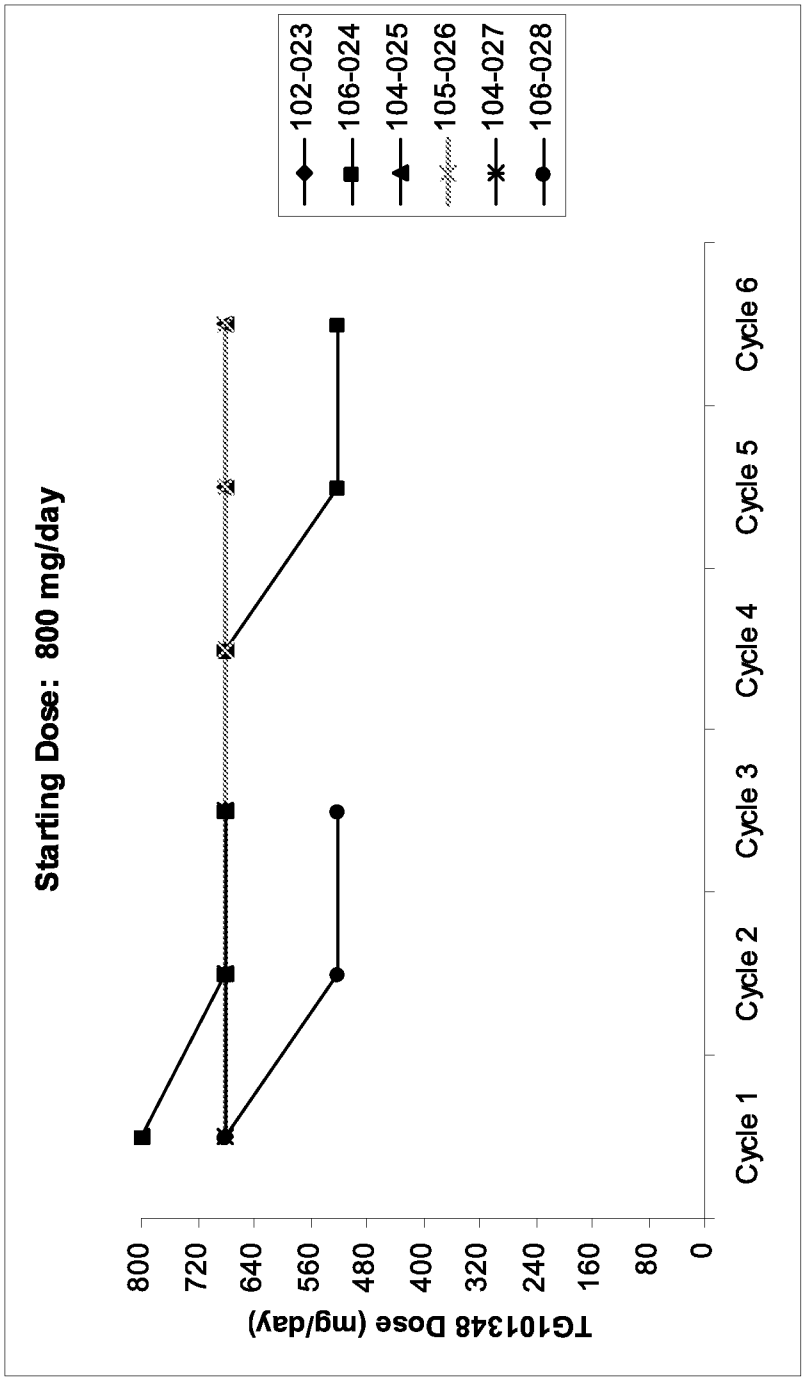

Starting Dose: 800 mg/day
TG101348 Dose (mg/day)
800
720
640
560
480
400
320
240
160
80
0
Cycle 1
Cycle 2
Cycle 3
Cycle 4
Cycle 5
Cycle 6
102-023
106-024
104-025
105-026
104-027
106-028

Figure 11

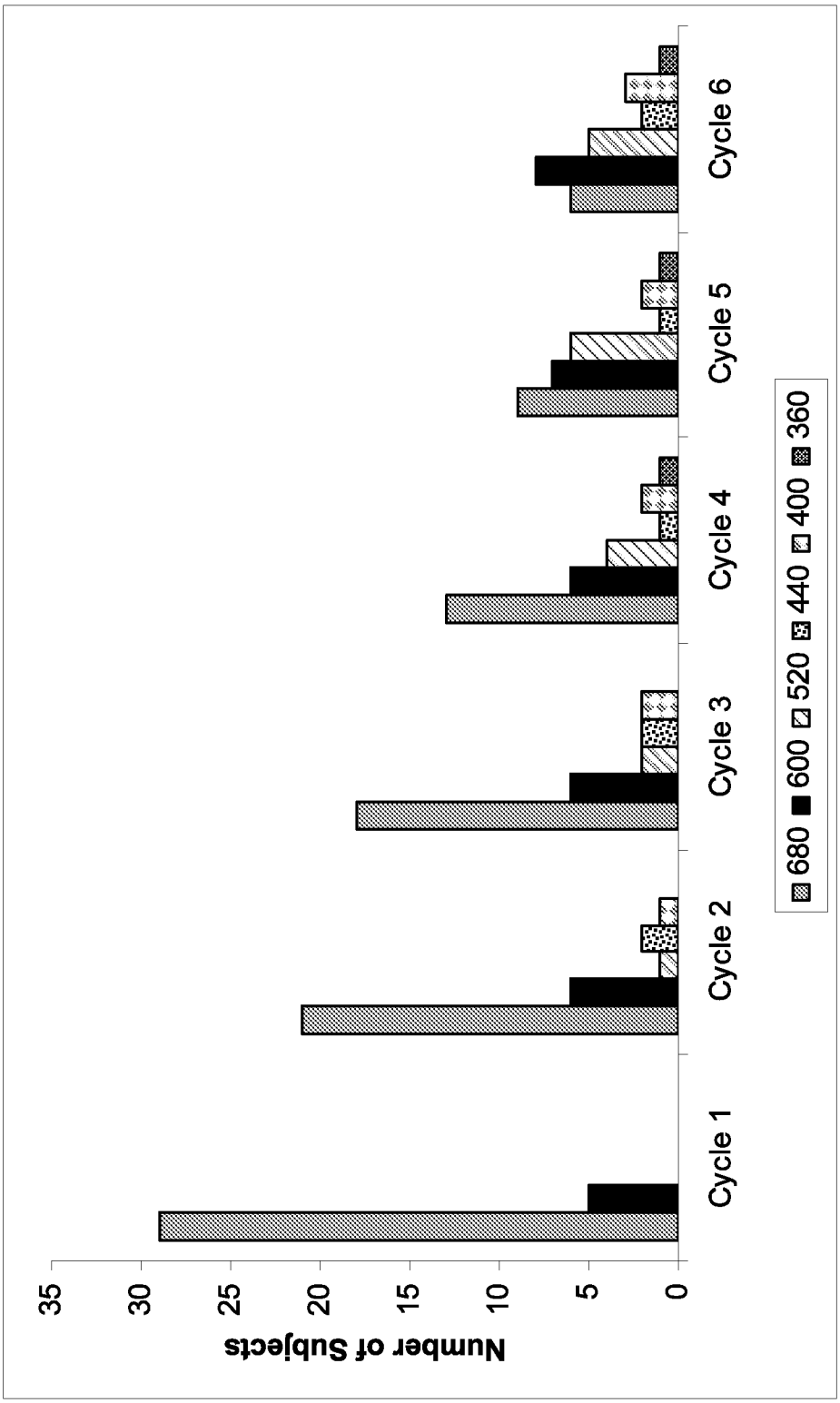

Number of Subjects
0
5
10
15
20
25
30
35
Cycle 1
Cycle 2
Cycle 3
Cycle 4
Cycle 5
Cycle 6
680
600
520
440
400
360

Figure 12A

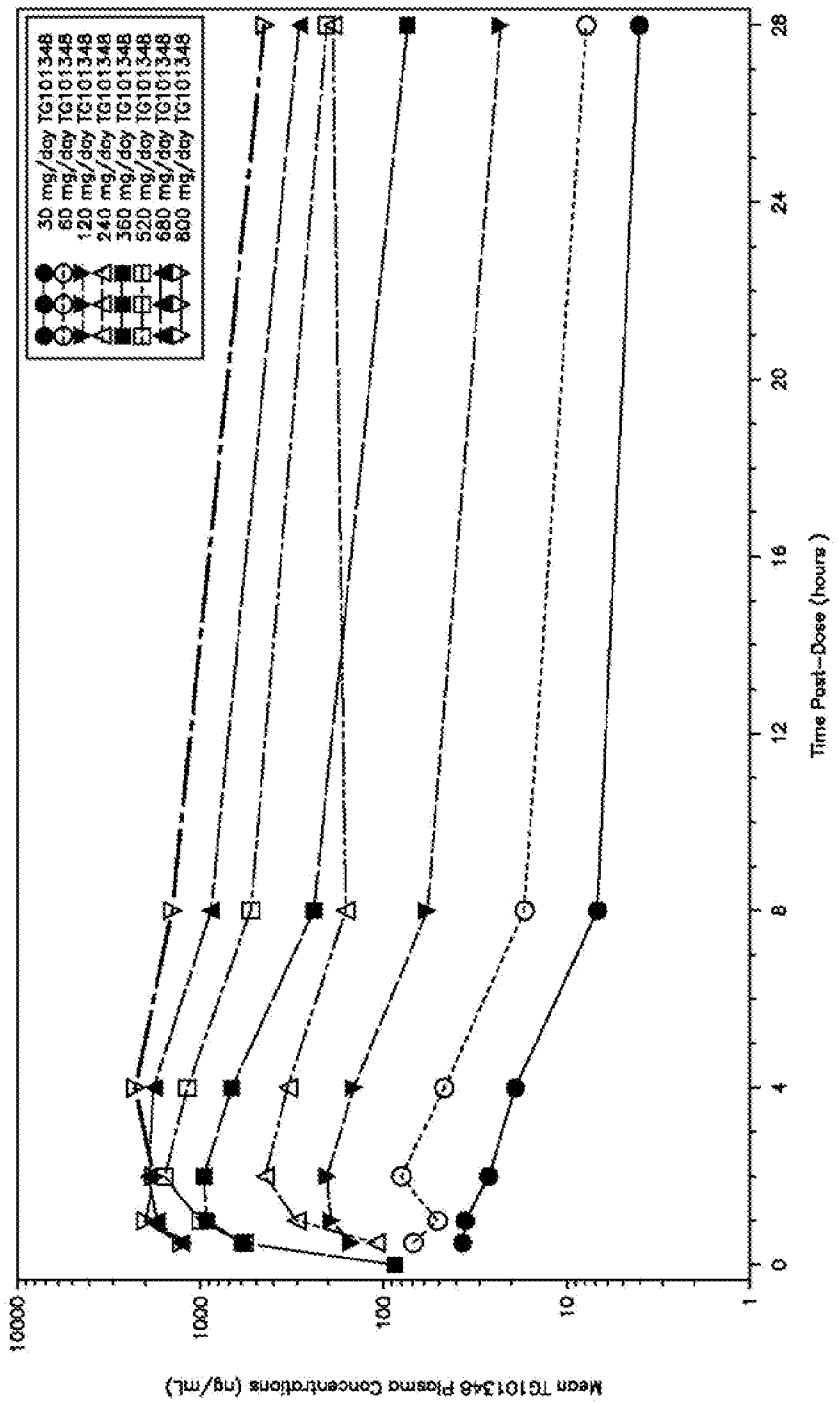

30 mg/day TG101348
60 mg/day TG101348
120 mg/day TG101348
240 mg/day TG101348
360 mg/day TG101348
520 mg/day TG101348
680 mg/day TG101348
800 mg/day TG101348
Mean TG101348 Plasma Concentrations (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
28
Time Post-Dose (hours)

Figure 12B

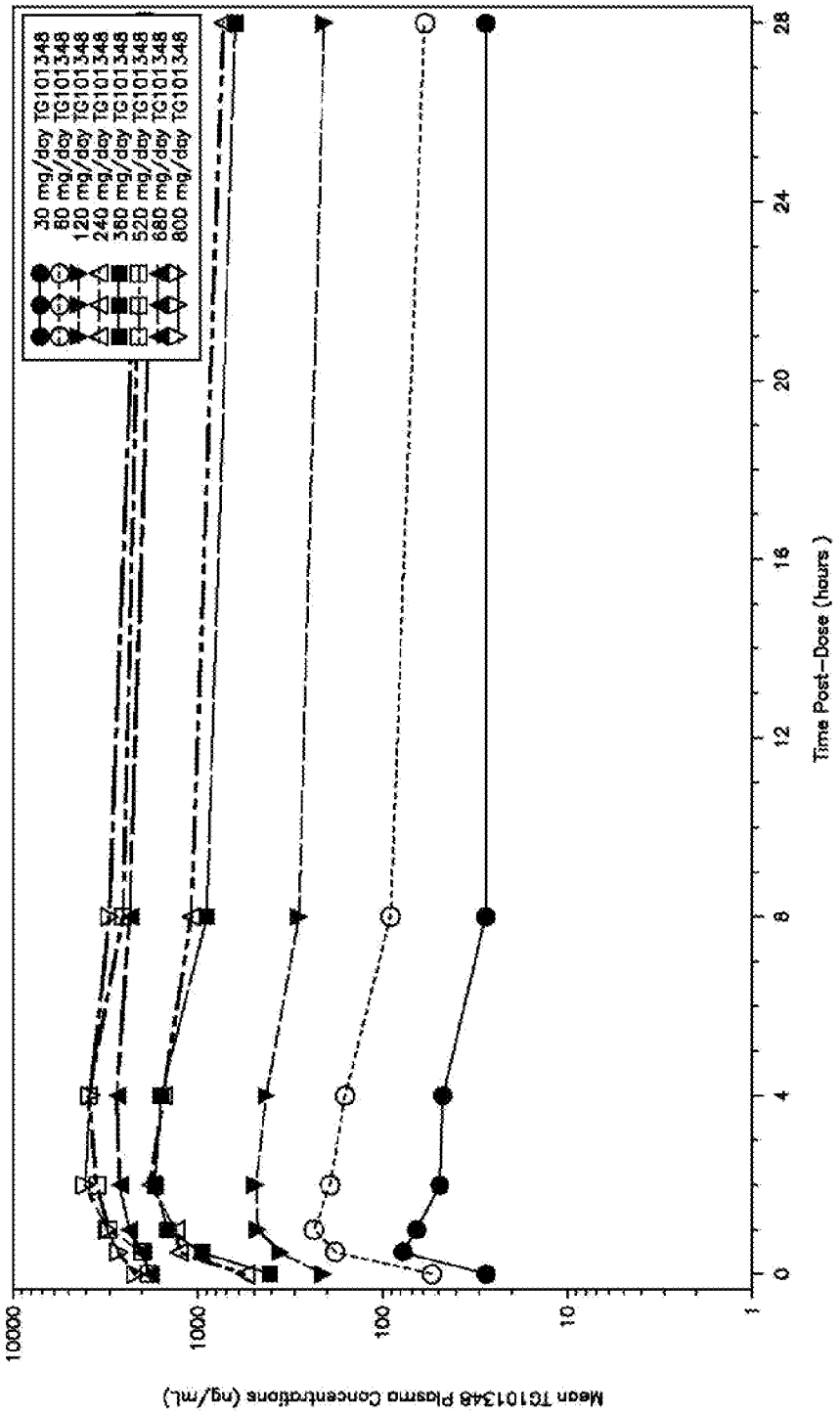
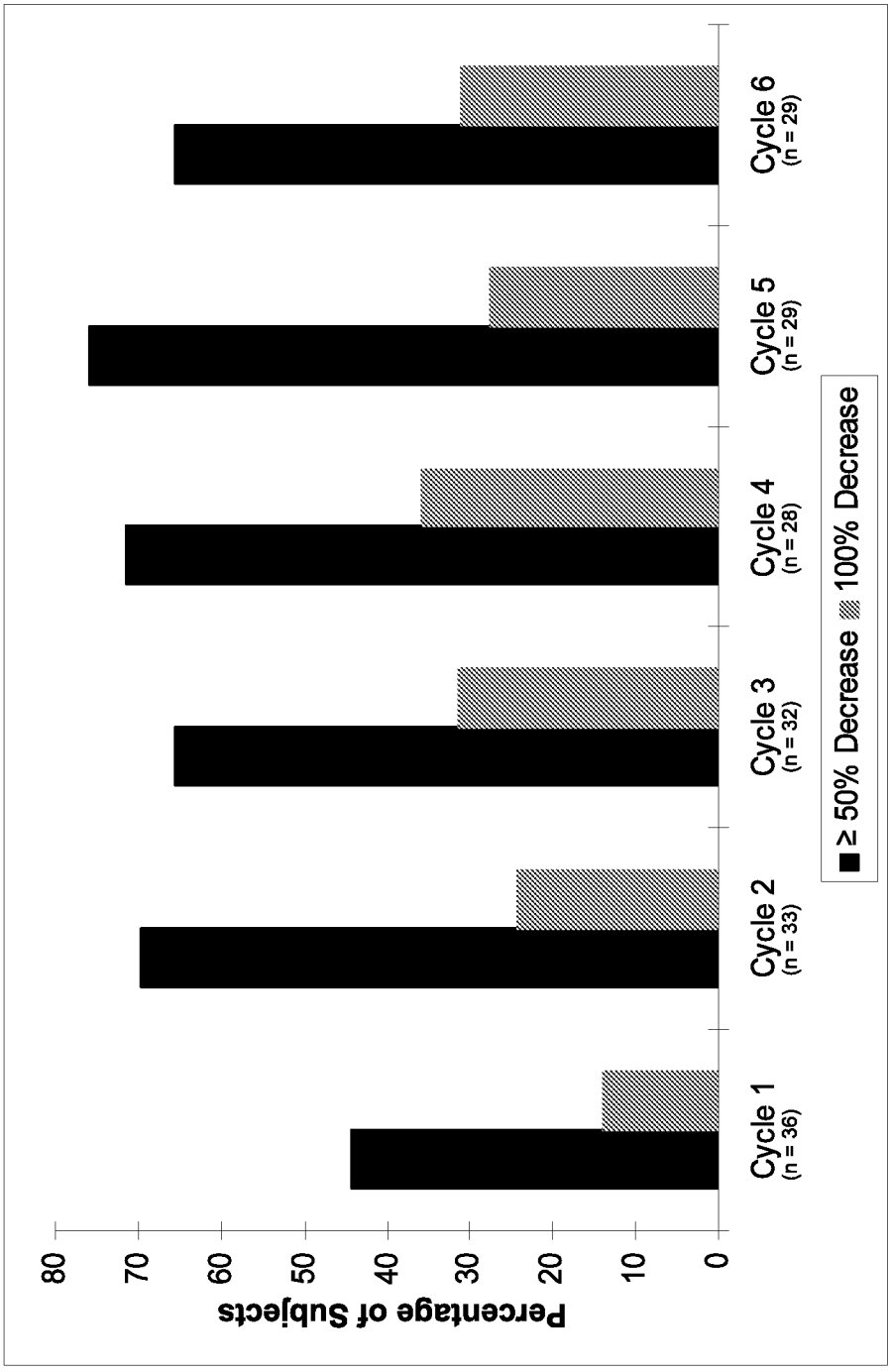

30 mg/day TG101348
60 mg/day TG101348
120 mg/day TG101348
240 mg/day TG101348
360 mg/day TG101348
520 mg/day TG101348
680 mg/day TG101348
800 mg/day TG101348
Mean TG101348 Plasma Concentrations (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
28
Time Post-Dose (hours)

Figure 13


Percentage of Subjects
0
10
20
30
40
50
60
70
80
Cycle 1 (n = 36)
Cycle 2 (n = 33)
Cycle 3 (n = 32)
Cycle 4 (n = 28)
Cycle 5 (n = 29)
Cycle 6 (n = 29)
≥ 50% Decrease
100% Decrease

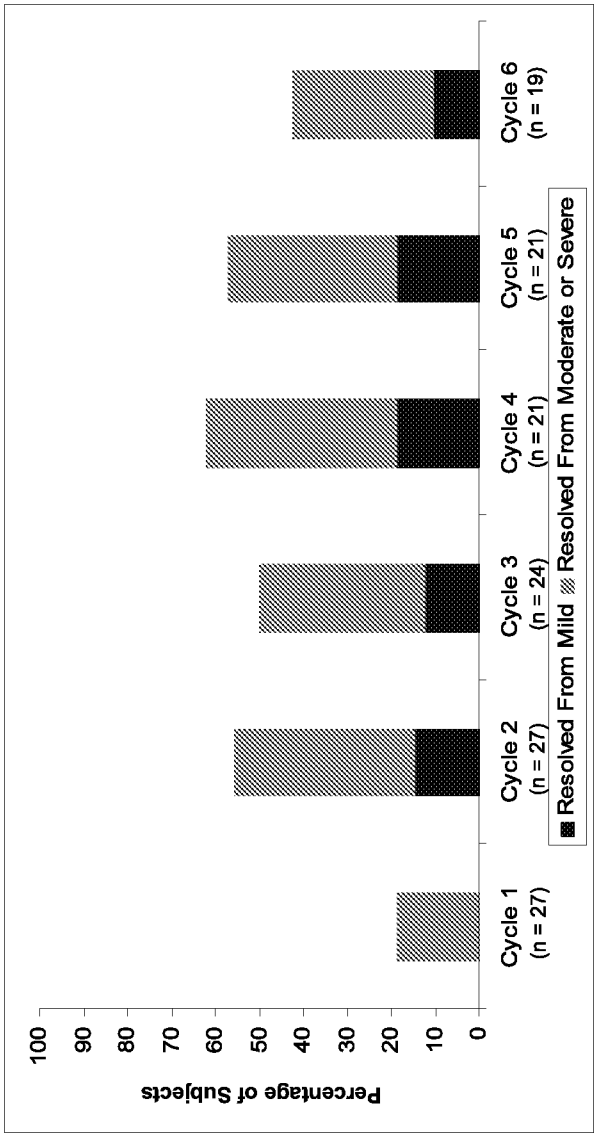


Figure 14A

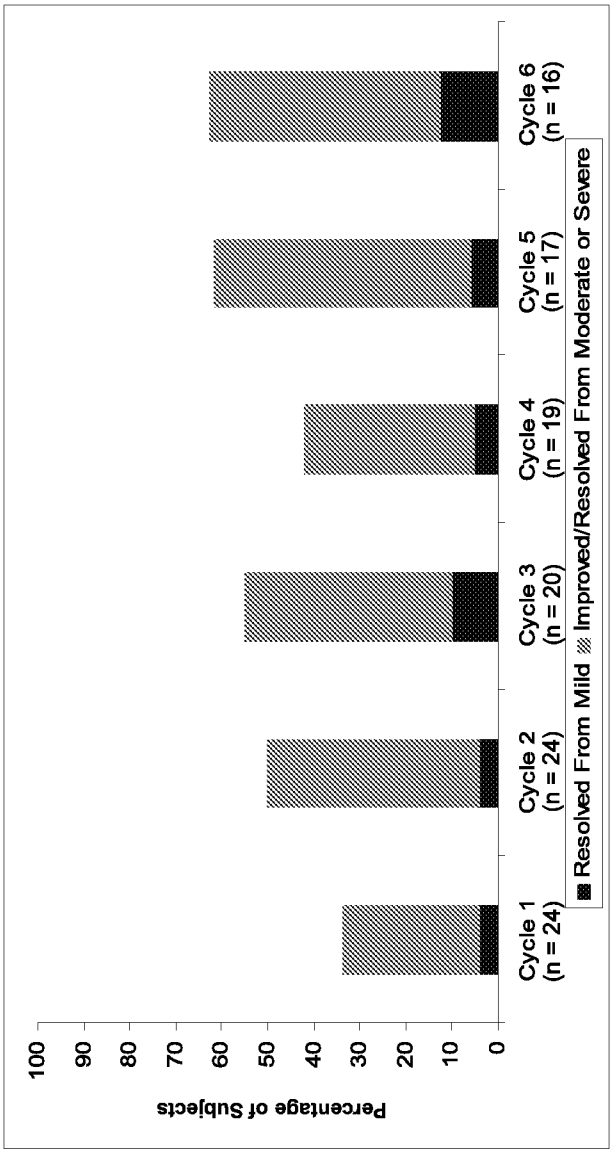


Figure 14B

Figure 14C

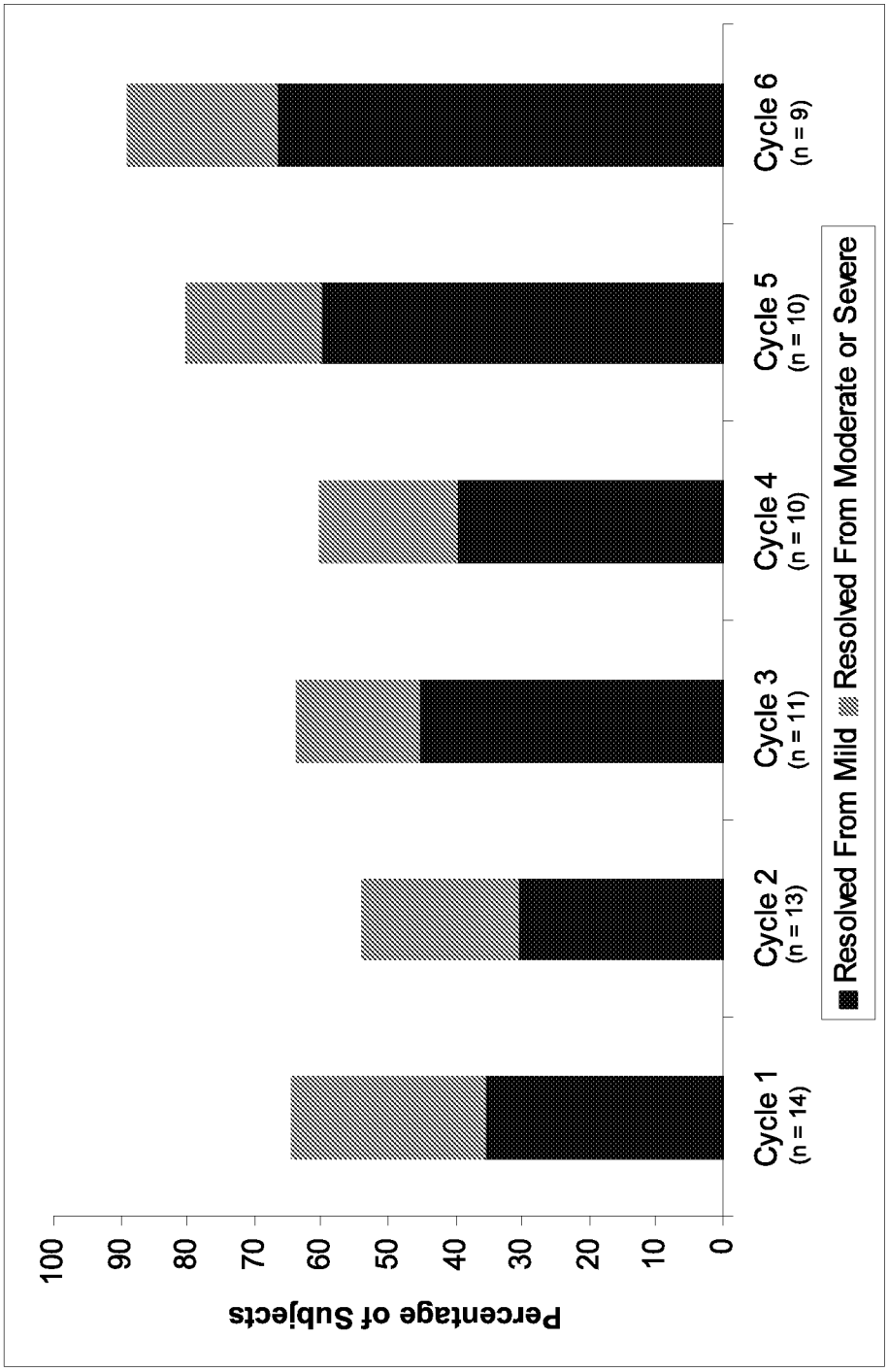
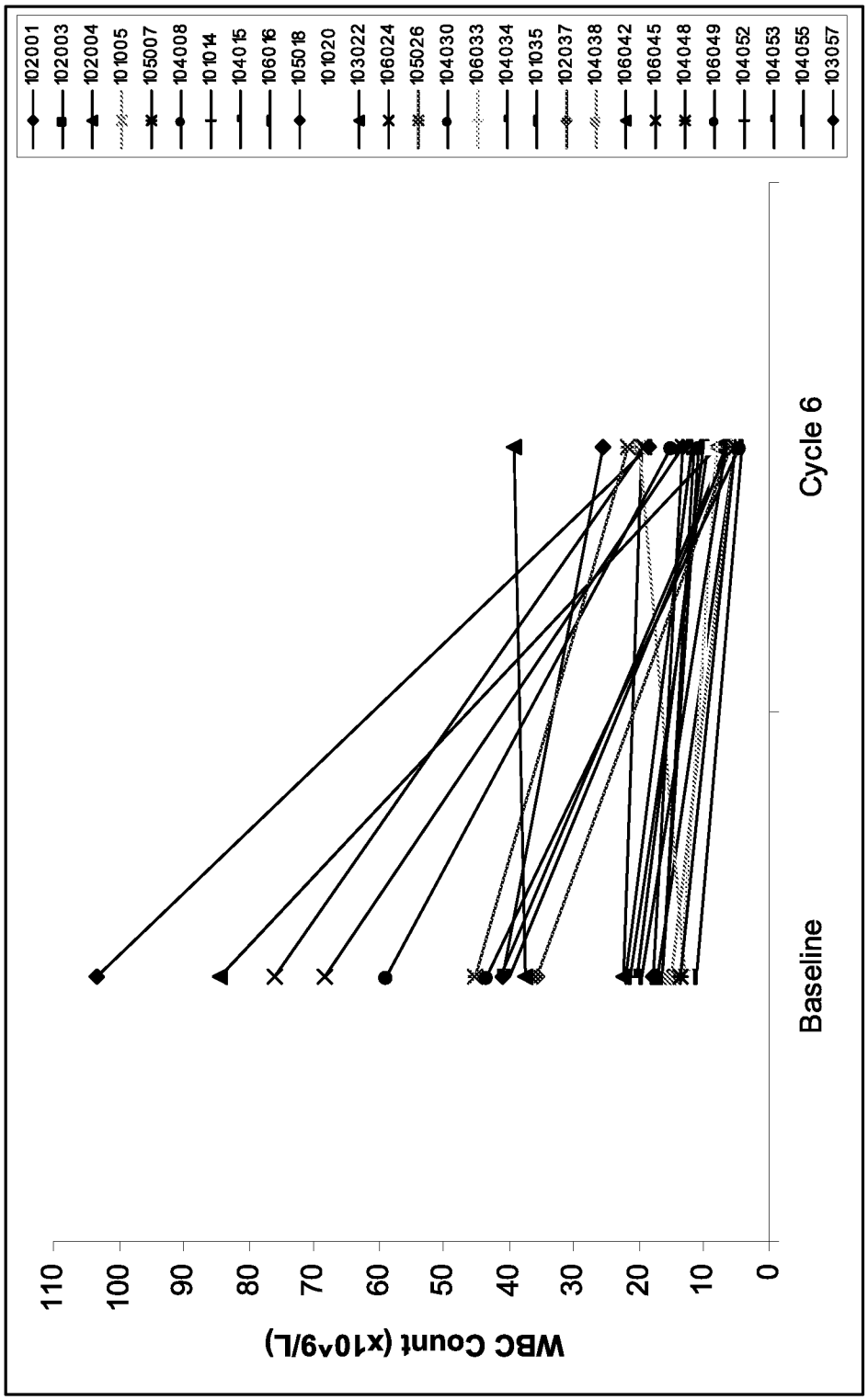

Percentage of Subjects
100
90
80
70
60
50
40
30
20
10
0
Cycle 1 (n = 14)
Cycle 2 (n = 13)
Cycle 3 (n = 11)
Cycle 4 (n = 10)
Cycle 5 (n = 10)
Cycle 6 (n = 9)
Resolved From Mild
Resolved From Moderate or Severe

Figure 15


102001
102003
102004
101005
105007
104008
101014
104015
106016
105018
101020
103022
106024
105026
104030
106033
104034
101035
102037
104038
106042
106045
104048
106049
104052
104053
104055
103057
WBC Count (x10^9/L)
110
100
90
80
70
60
50
40
30
20
10
0
Baseline
Cycle 6

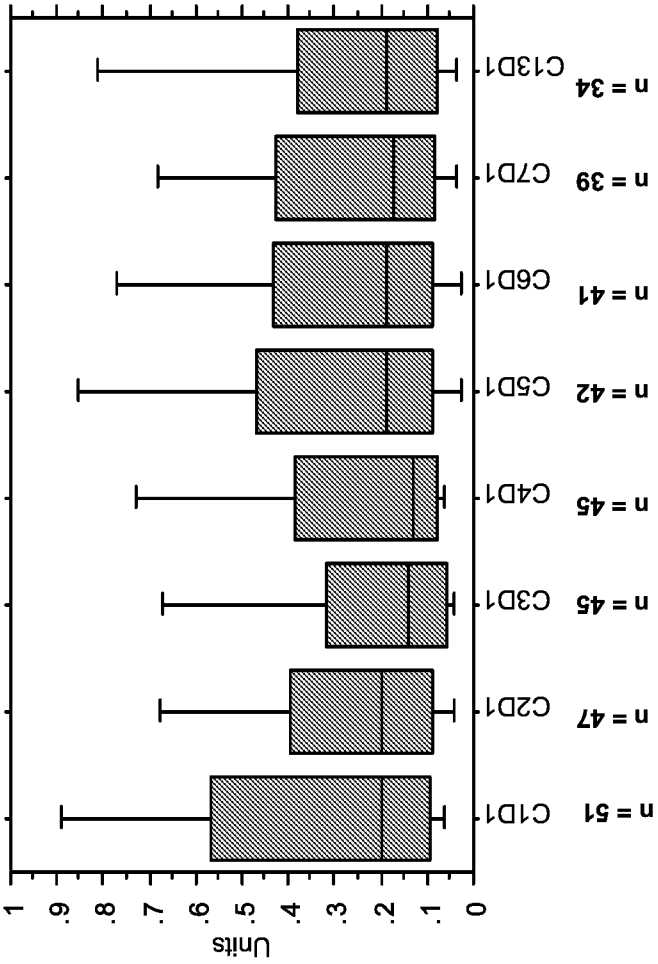


Figure 16A

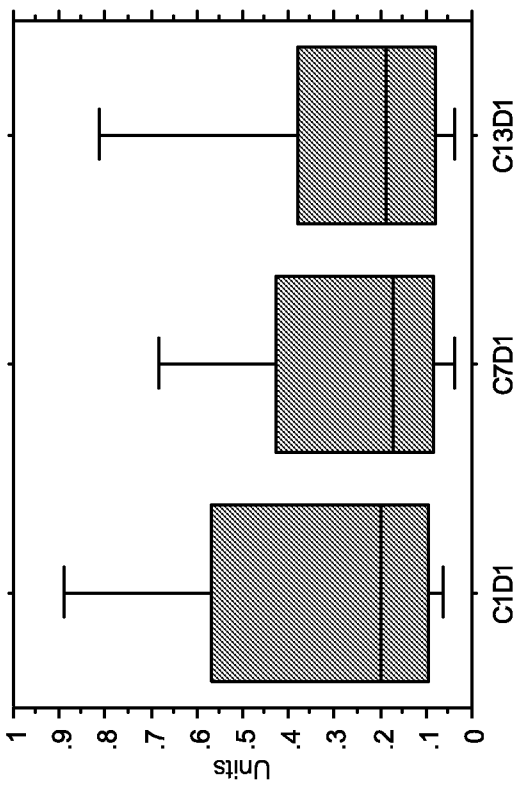


Figure 16B

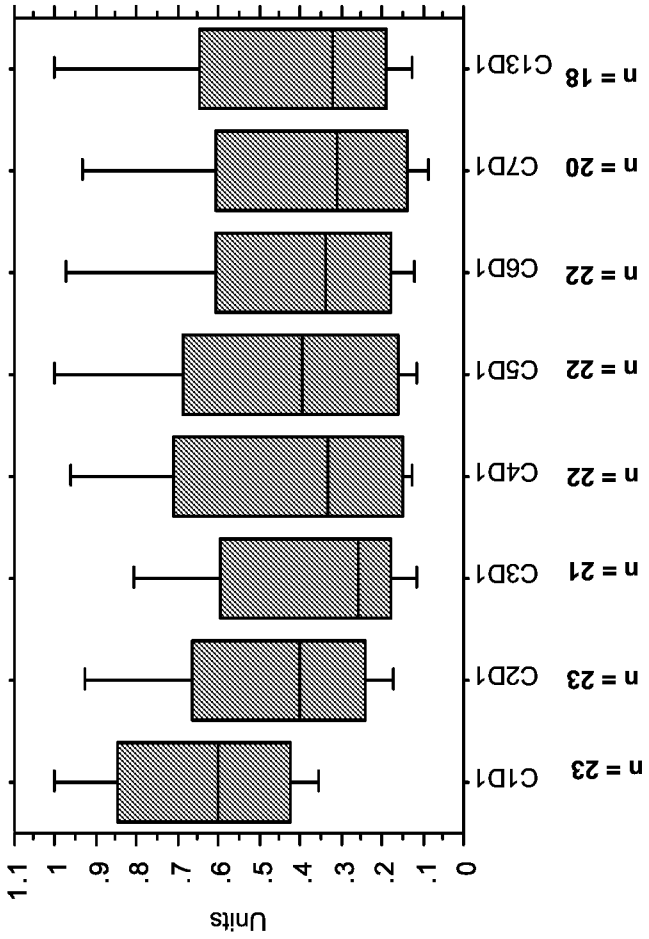


Figure 16C

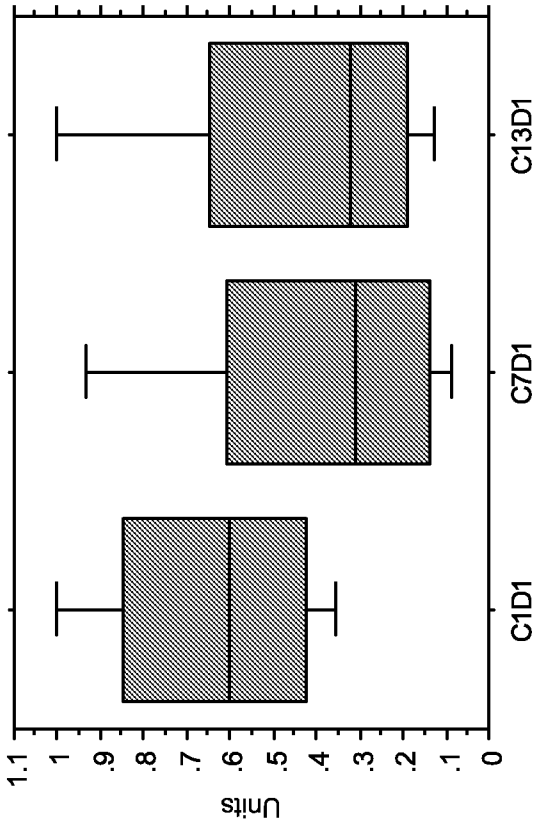
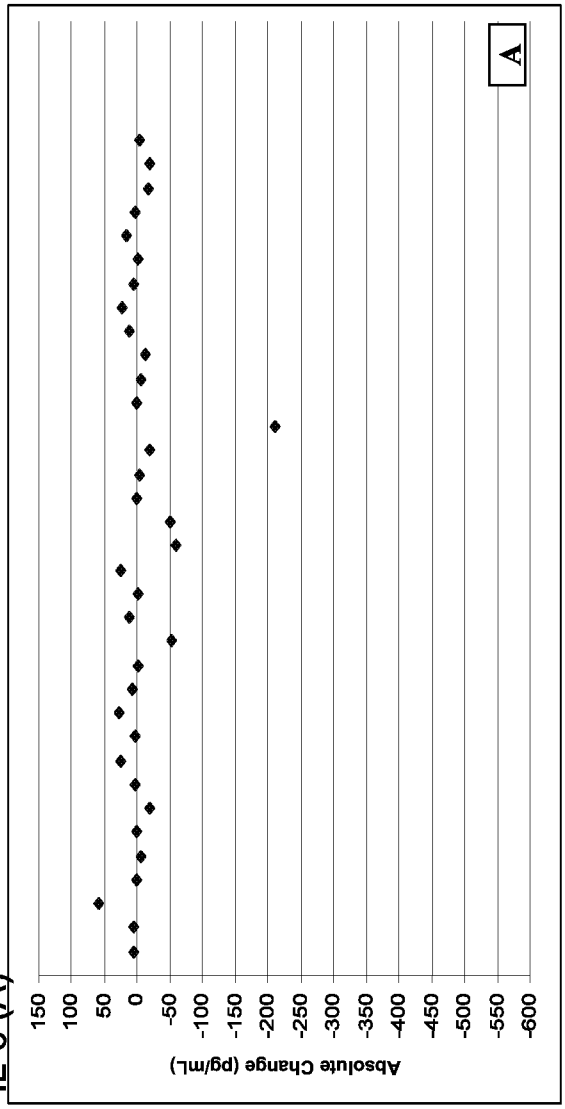


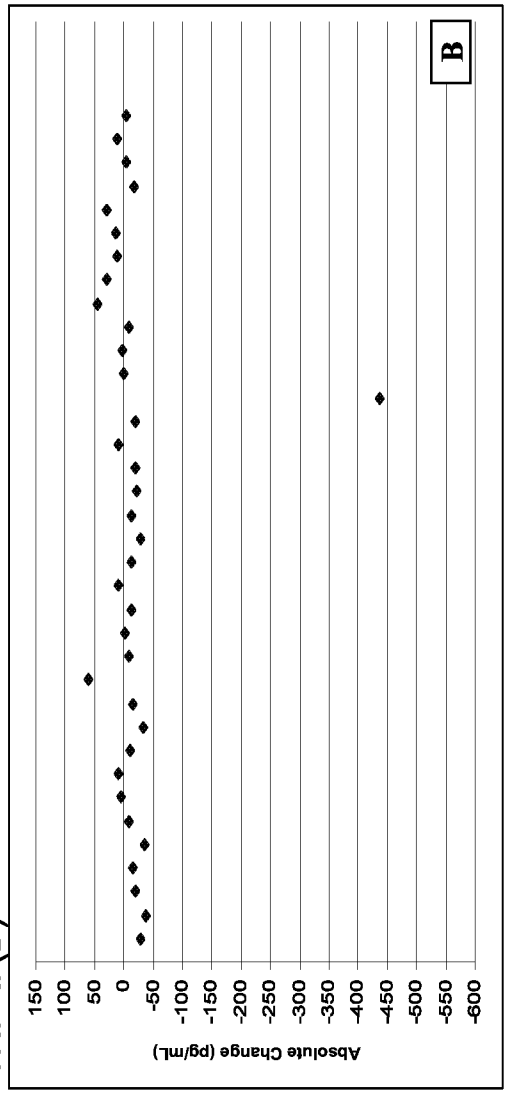
Figure 16D

Figure 17A



Absolute differences in IL-6 (-4719 pg/mL) and IL-2 (-1827 pg/mL) are omitted from panels A and D, respectively, for 1 subject (101-039) because they skewed presentation of data for other subjects.

Figure 17B



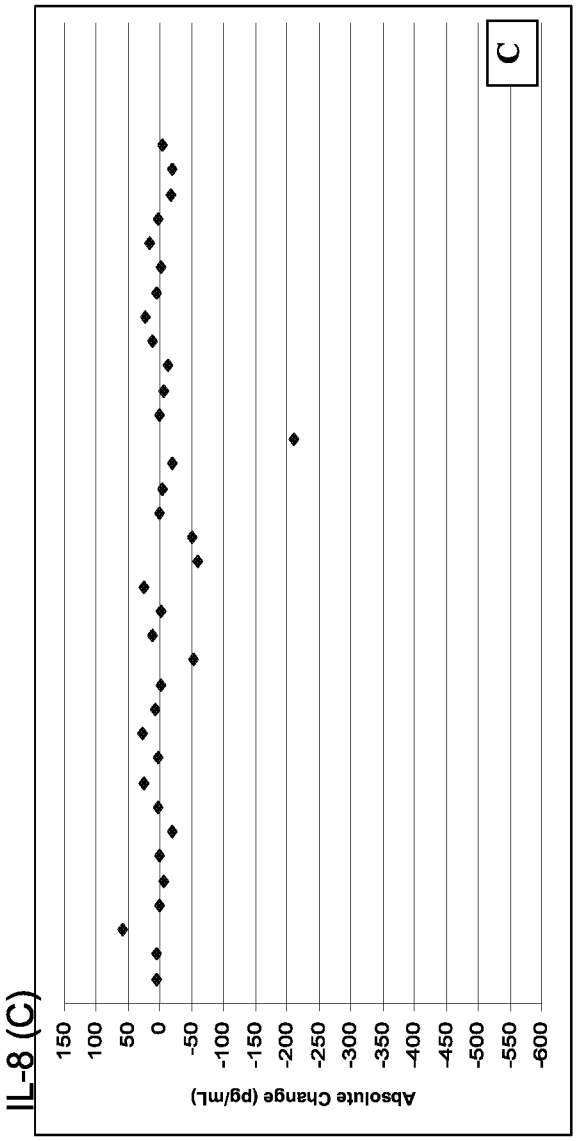


Figure 17C

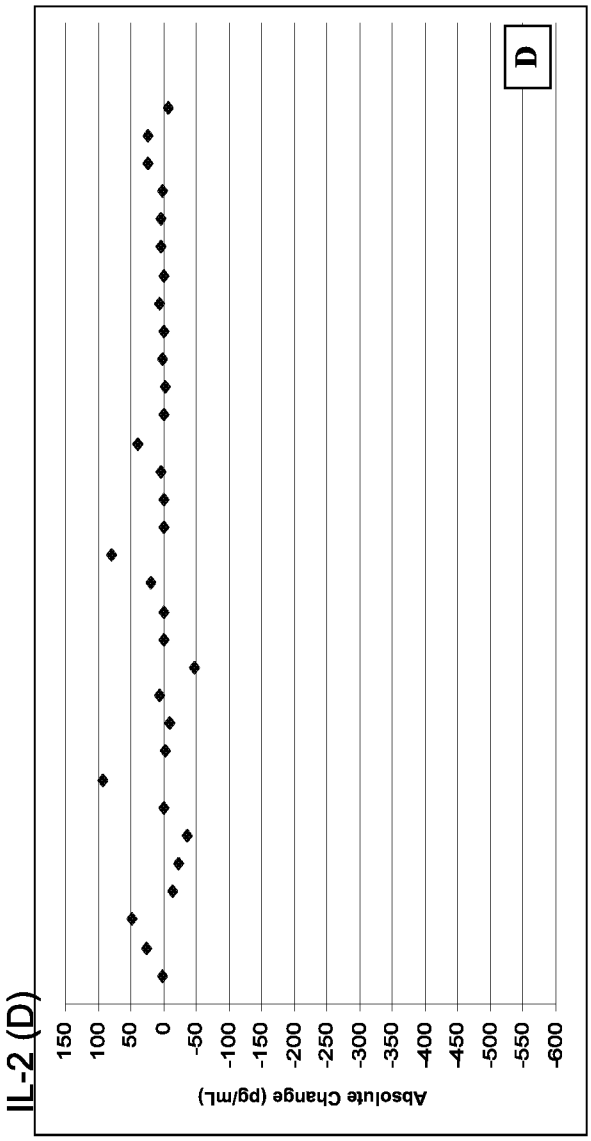
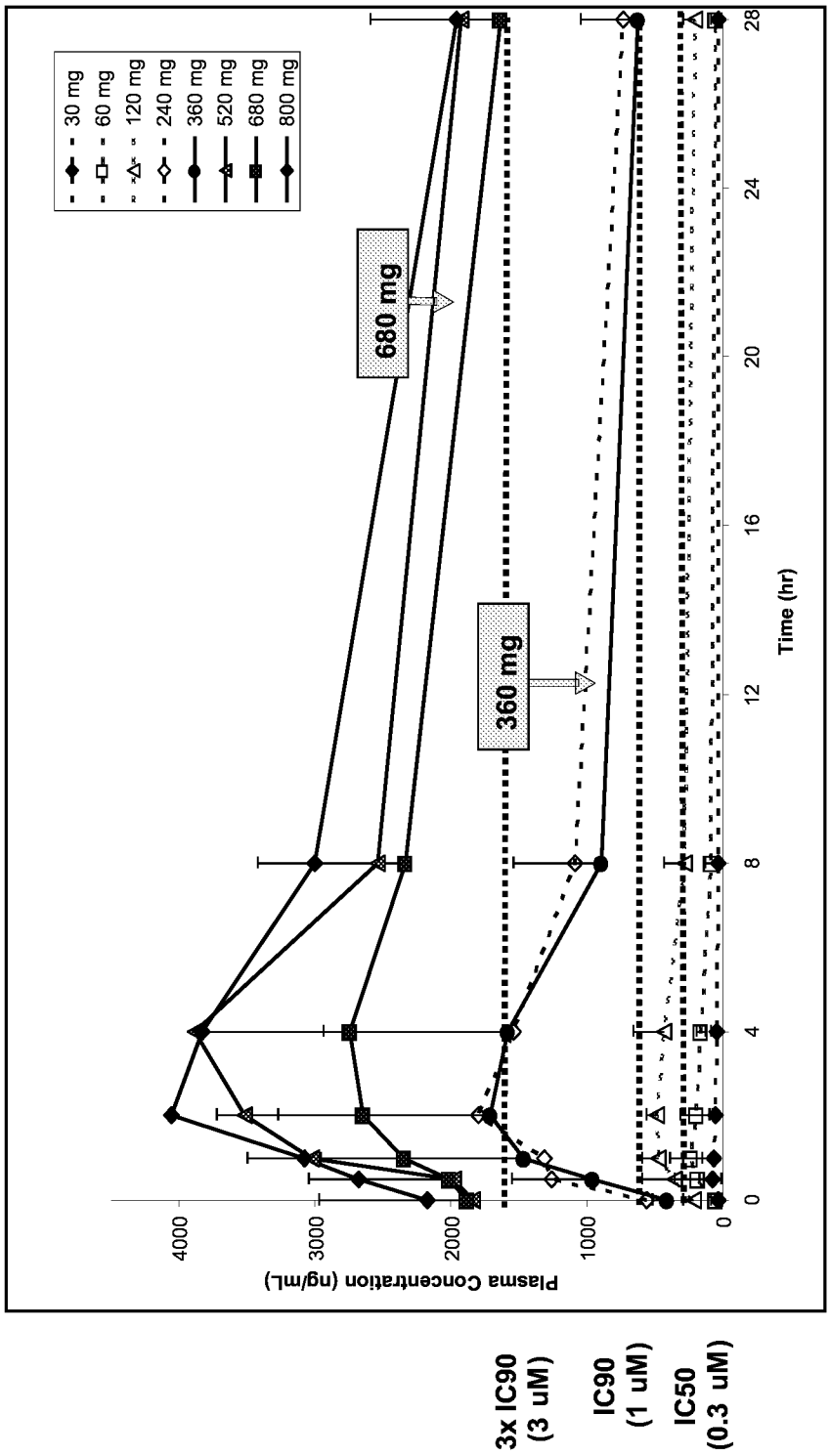


Figure 17D

Figure 18


30 mg
60 mg
120 mg
240 mg
360 mg
520 mg
680 mg
800 mg
680 mg
360 mg
Plasma Concentration (ng/mL)
Time (hr)
3x IC90 (3 uM)
IC90 (1 uM)
IC50 (0.3 uM)