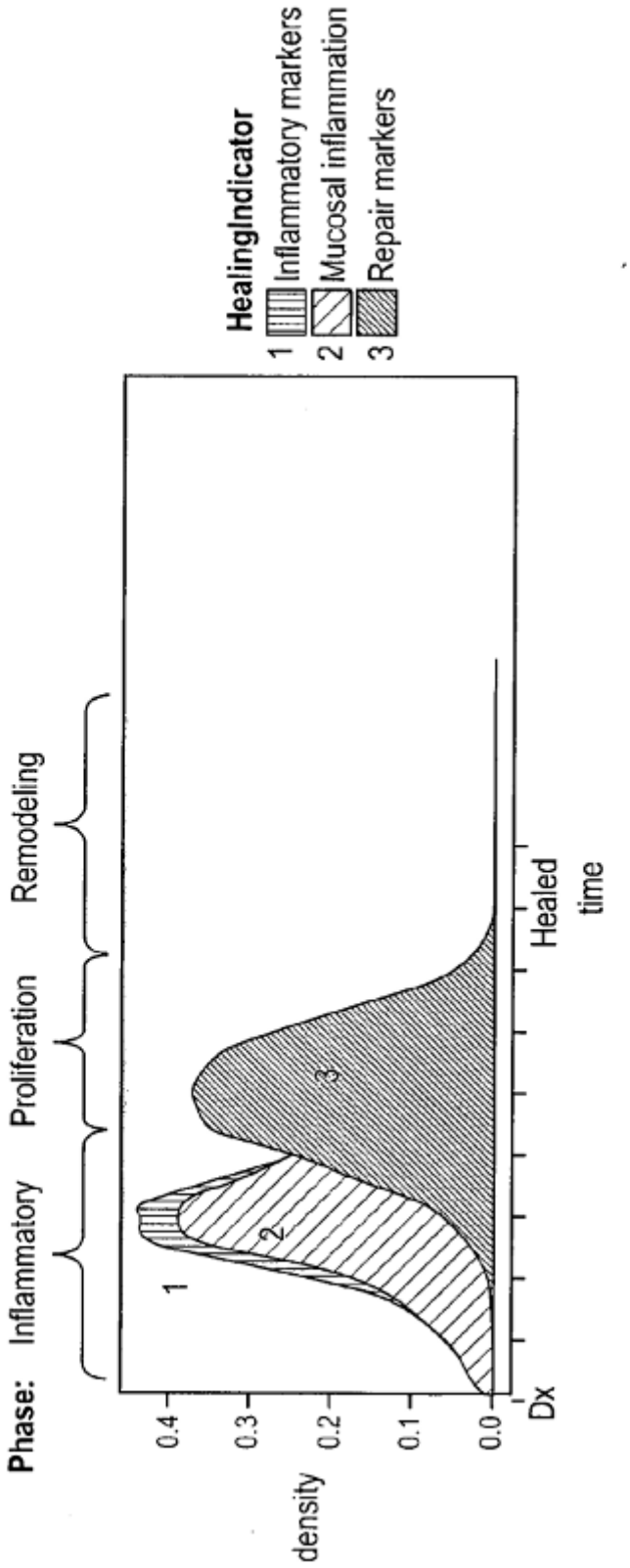

HealingIndicator
1 Inflammatory markers
2 Mucosal inflammation
3 Repair markers
Phase: Inflammatory Proliferation Remodeling
density
0.4
0.3
0.2
0.1
0.0
Dx
Healed
time
1
2
3

FIG. 1

FIG. 2A

Mucosal improvement measured at each scope per individual:

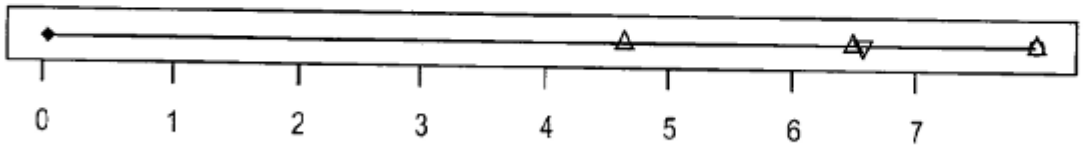


Years Since Diagnosis

◆ Diagnosis
△ Sample
○ Scope-Not Healed
× Scope-Marked Improvement
▽ Scope-Complete Improvement

FIG. 2B

However, some individuals 'relapse' after complete improvement:



Years Since Diagnosis

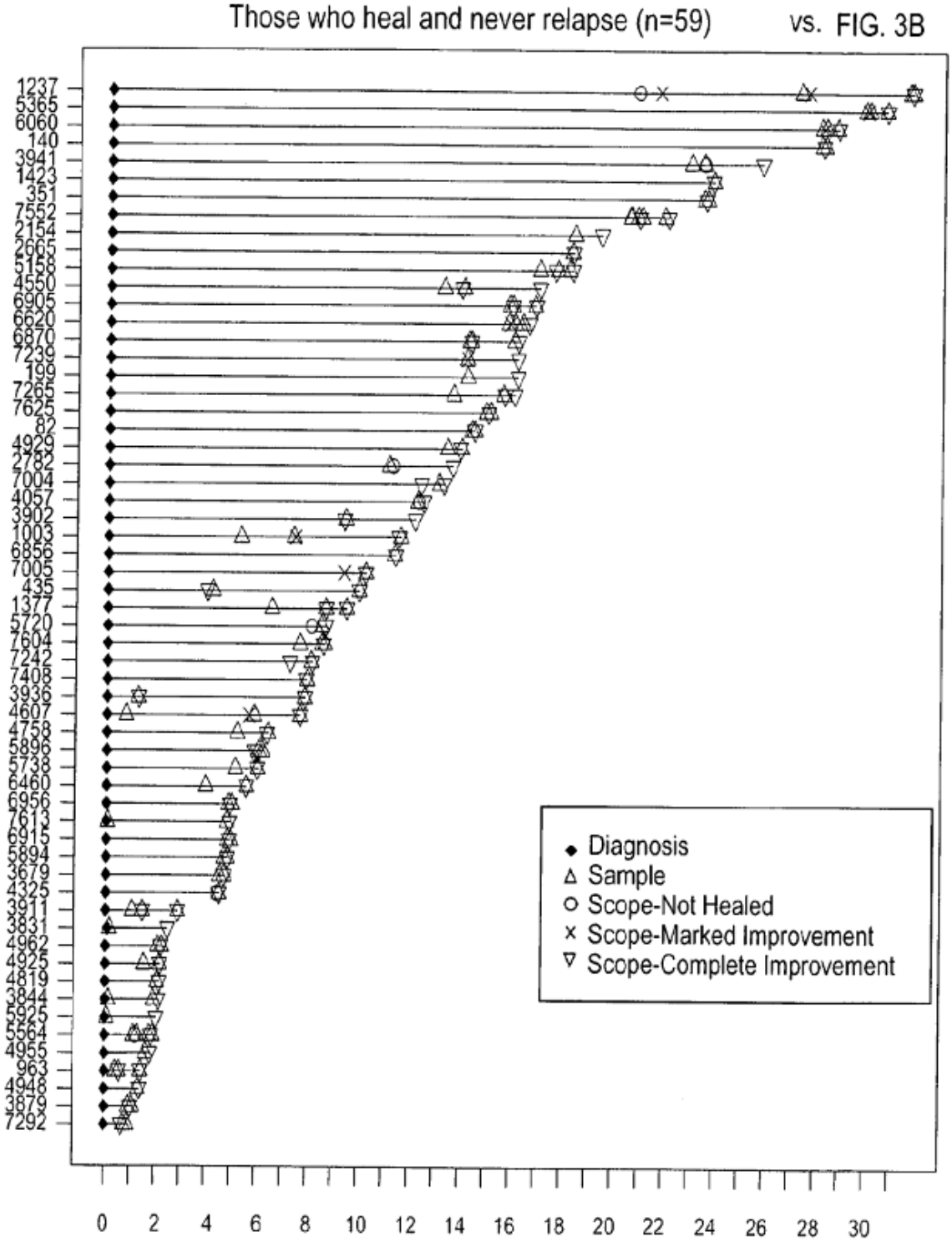

Those who heal and never relapse (n=59)
vs. FIG. 3B
1237
5365
6060
140
3941
1423
351
7552
2154
2665
5158
4550
6905
6620
6870
7238
199
7265
7625
82
4929
2782
7004
4057
3902
1003
6856
7005
435
1377
5720
7604
7242
7408
3936
4607
4758
5896
5738
6460
6956
7613
6915
5894
3679
4325
3911
3831
4962
4925
4819
3844
5925
5564
4955
963
4948
3679
7292
Diagnosis
Sample
Scope-Not Healed
Scope-Marked Improvement
Scope-Complete Improvement
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
Years Since Diagnosis

FIG. 3A

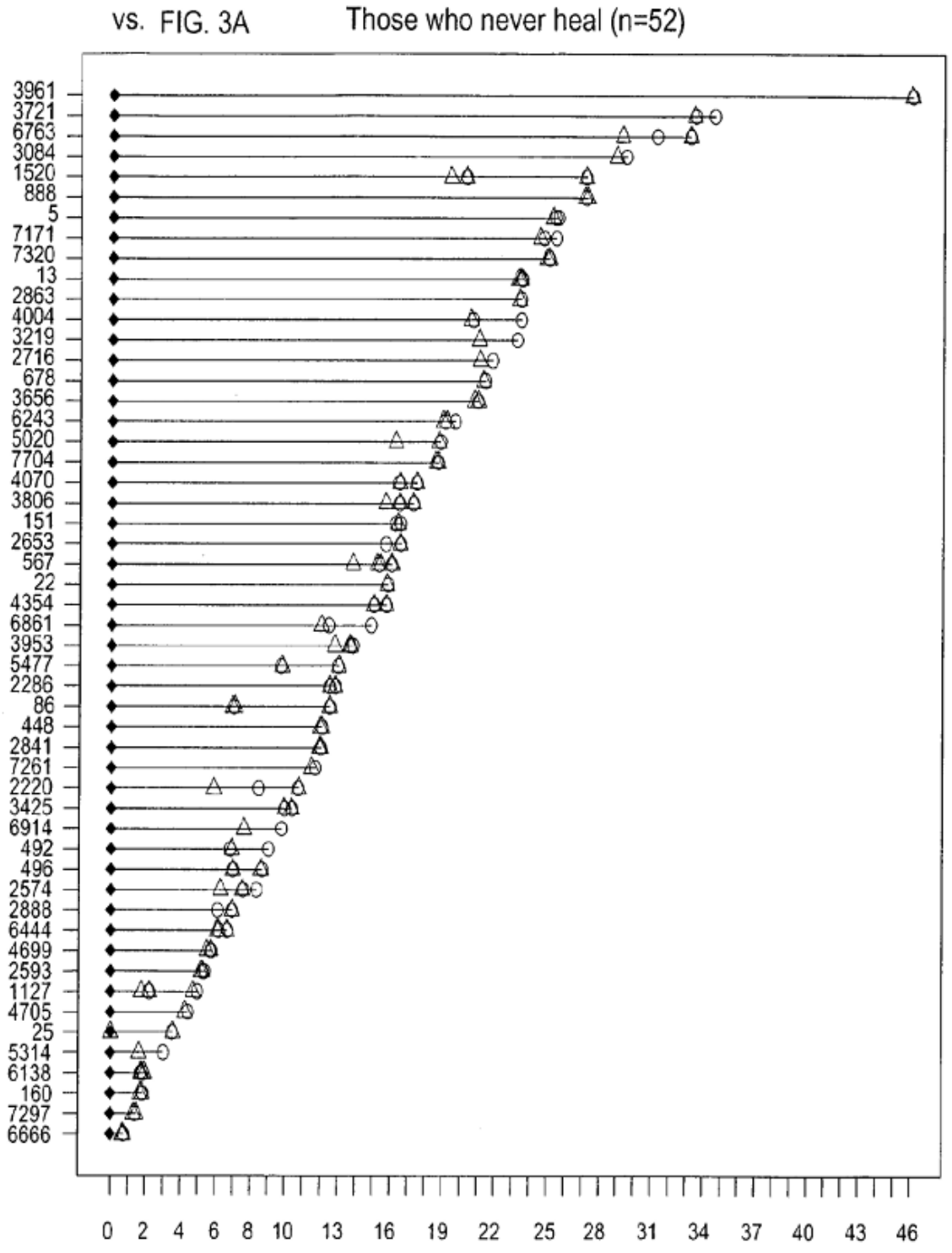

vs. FIG. 3A
Those who never heal (n=52)
3961
3721
6763
3084
1520
888
5
7171
7320
13
2863
4004
3219
2716
678
3656
6243
5020
7704
4070
3806
151
2653
567
22
4354
6861
3953
5477
2286
86
448
2841
7261
2220
3425
6914
492
496
2574
2888
6444
4699
2593
1127
4705
25
5314
6138
160
7297
6666
0 2 4 6 8 10 13 16 19 22 25 28 31 34 37 40 43 46
Years Since Diagnosis

FIG. 3B

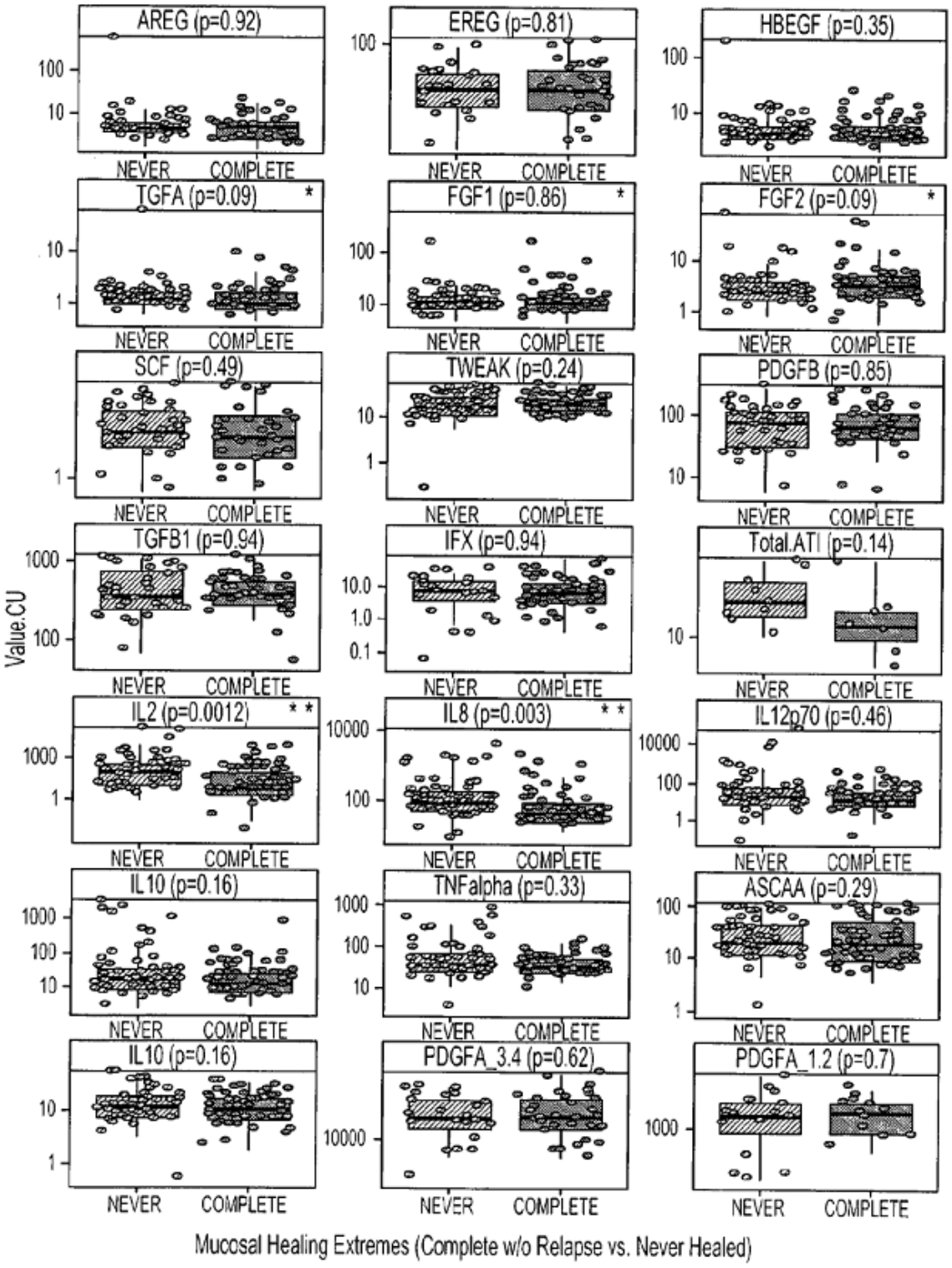

AREG (p=0.92)
EREG (p=0.81)
HBEGF (p=0.35)
TGFA (p=0.09) *
FGF1 (p=0.86) *
FGF2 (p=0.09) *
SCF (p=0.49)
TWEAK (p=0.24)
PDGFB (p=0.85)
TGFB1 (p=0.94)
IFX (p=0.94)
Total.ATI (p=0.14)
IL2 (p=0.0012) **
IL8 (p=0.003) **
IL12p70 (p=0.46)
IL10 (p=0.16)
TNFalpha (p=0.33)
ASCAA (p=0.29)
IL10 (p=0.16)
PDGFA_3.4 (p=0.62)
PDGFA_1.2 (p=0.7)
NEVER
COMPLETE
Value.CU
Mucosal Healing Extremes (Complete w/o Relapse vs. Never Healed)

FIG. 4

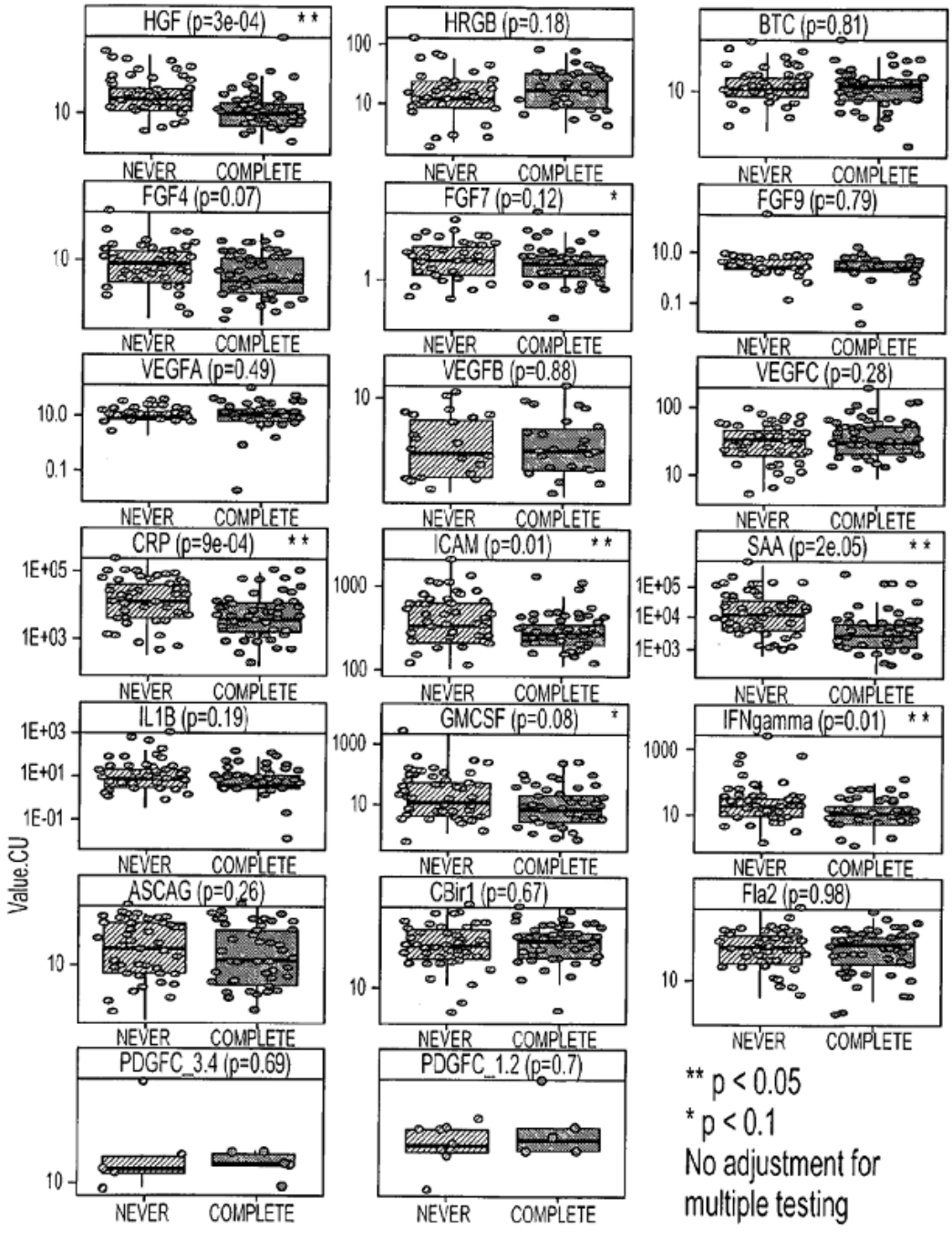
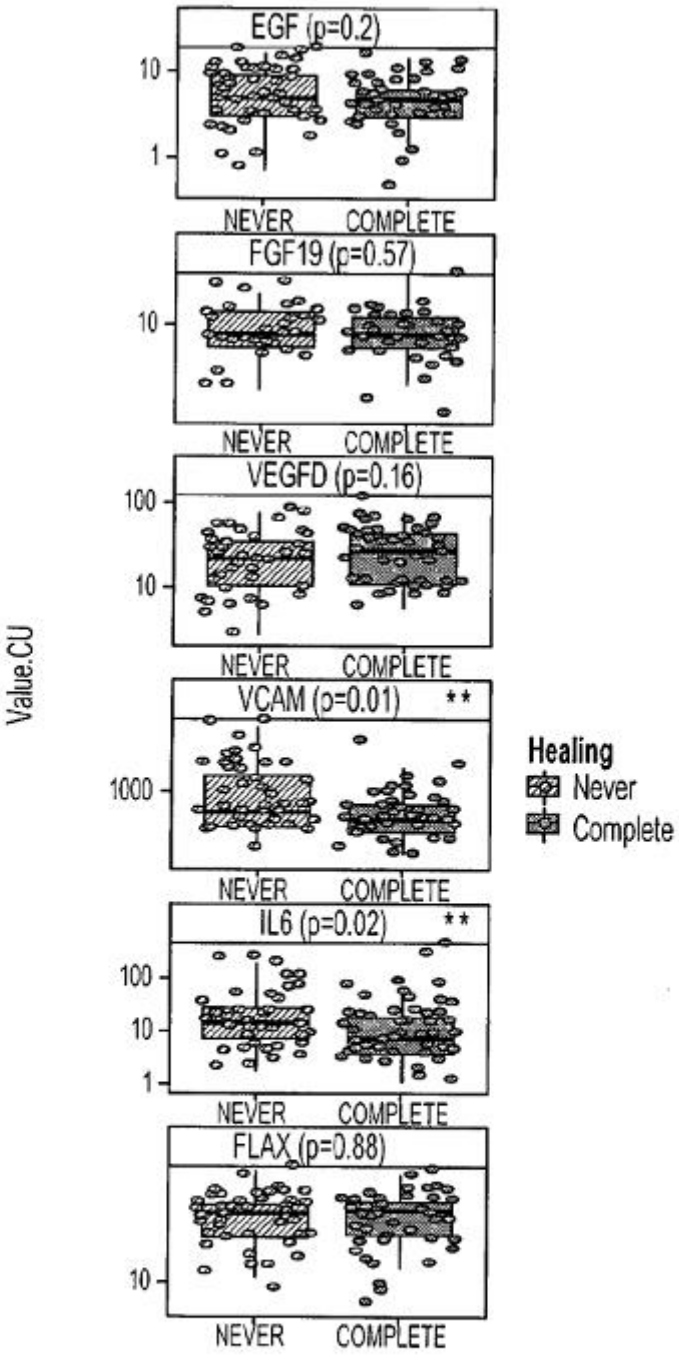

HGF (p=3e-04) **
HRGB (p=0.18)
BTC (p=0.81)
FGF4 (p=0.07)
FGF7 (p=0.12) *
FGF9 (p=0.79)
VEGFA (p=0.49)
VEGFB (p=0.88)
VEGFC (p=0.28)
CRP (p=9e-04) **
ICAM (p=0.01) **
SAA (p=2e.05) **
IL1B (p=0.19)
GMCSF (p=0.08) *
IFNgamma (p=0.01) **
ASCAG (p=0.26)
CBir1 (p=0.67)
Fla2 (p=0.98)
PDGFC_3.4 (p=0.69)
PDGFC_1.2 (p=0.7)
NEVER
COMPLETE
Value.CU
** p < 0.05
* p < 0.1
No adjustment for multiple testing
Mucosal Healing Extremes (Complete w/o Relapse vs. Never Healed)

FIG. 4 (CONT.)



Mucosal Healing Extremes (Complete w/o Relapse vs. Never Healed)

FIG. 4 (CONT.)

Marker	Odds Ratio (95% CI)	p value
GMCSF	0.9837 (0.9698 - 0.9978)	0.024
IL2	0.9921 (0.9844 - 0.9998)	0.046
VCAM	0.9995 (0.9990 - 0.9999)	0.026
HGF	0.9095 (0.8414 - 0.9831)	0.017

FIG. 5

FIG. 6A

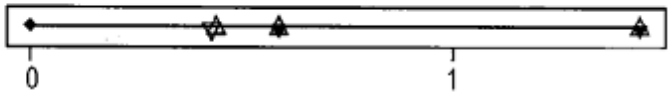
'True' healed individuals

Identified by:

1. Samples paired with one 'no improvement' scope followed by two 'complete improvement' scopes (e.g., BELOW)
2. **Inflammation low or decreasing over time**

SEE FIG. 7

N = 4



Years Since Diagnosis

vs.

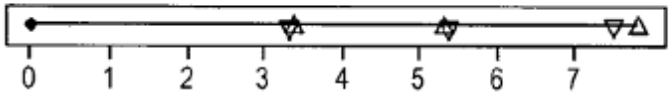
FIG. 6B

Not healed individuals

Identified by:

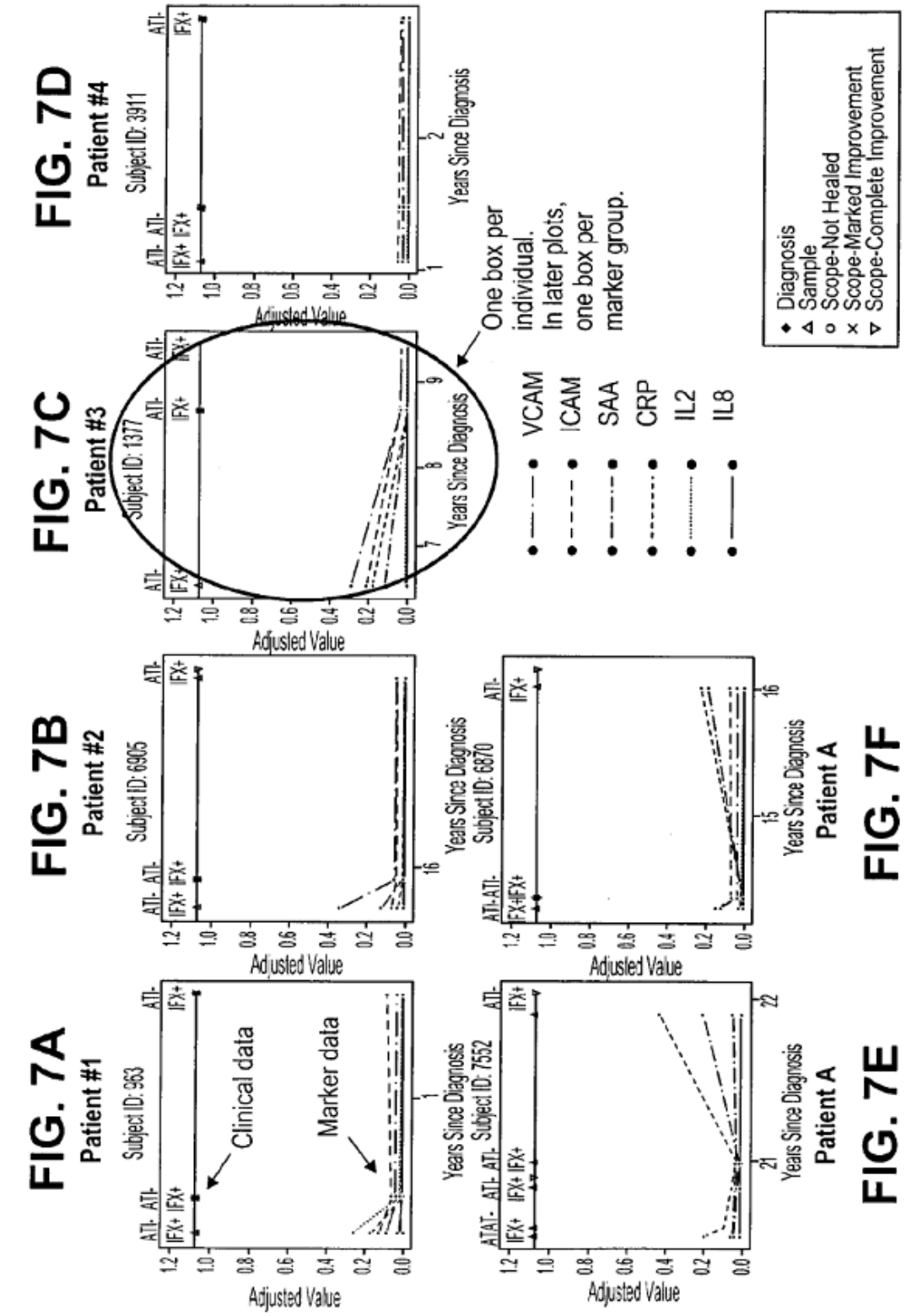
1. Samples paired with three 'no improvement' scopes (e.g., BELOW)
2. Total length of time between first and last events similar to 'true' healed individuals

N = 4



Years Since Diagnosis

◆ Diagnosis
△ Sample
▽ Scope-Not Healed
▼ Scope-Marked Improvement
▼ Scope-Complete Improvement


FIG. 7A
Patient #1
Subject ID: 963
Clinical data
Marker data
Adjusted Value
Years Since Diagnosis
FIG. 7B
Patient #2
Subject ID: 6905
FIG. 7C
Patient #3
Subject ID: 1377
FIG. 7D
Patient #4
Subject ID: 3911
One box per individual. In later plots, one box per marker group.
VCAM
ICAM
SAA
CRP
IL2
IL8
Diagnosis
Sample
Scope-Not Healed
Scope-Marked Improvement
Scope-Complete Improvement
FIG. 7E
Patient A
Subject ID: 7552
FIG. 7F
Patient A
Subject ID: 6870

Patient #1

FIG. 8A

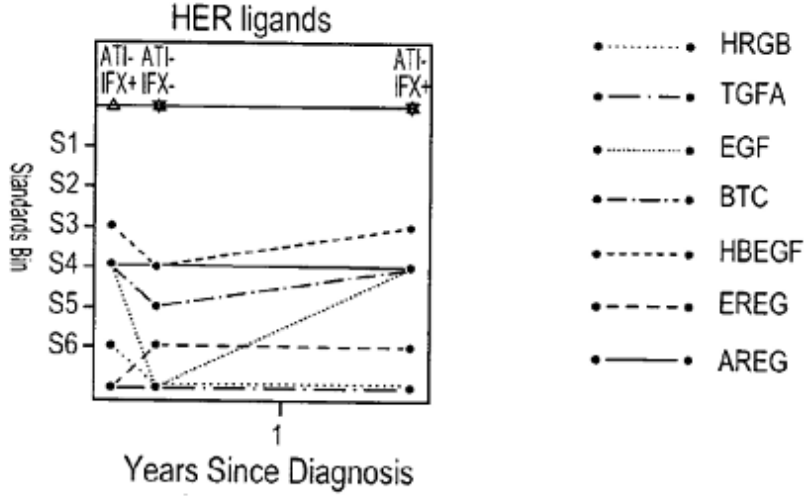
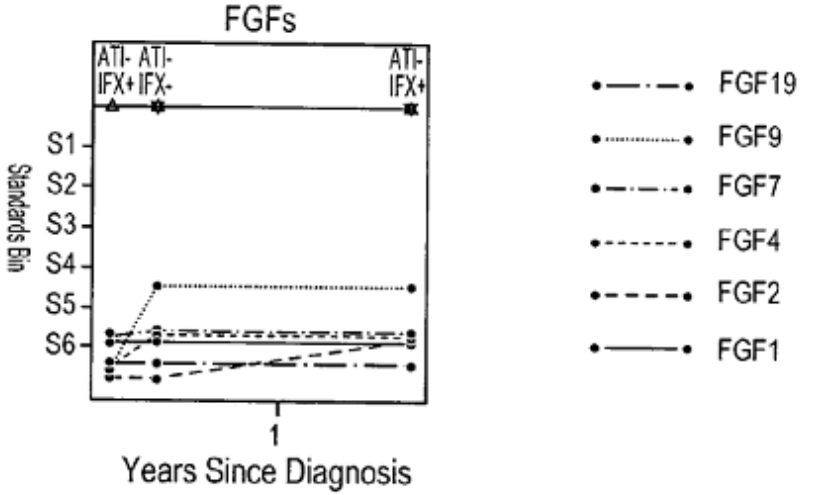


FIG. 8B



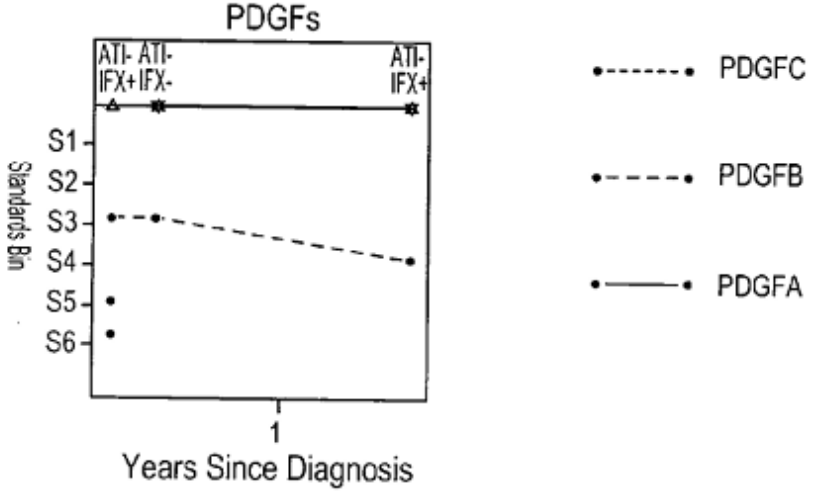


FIG. 8C

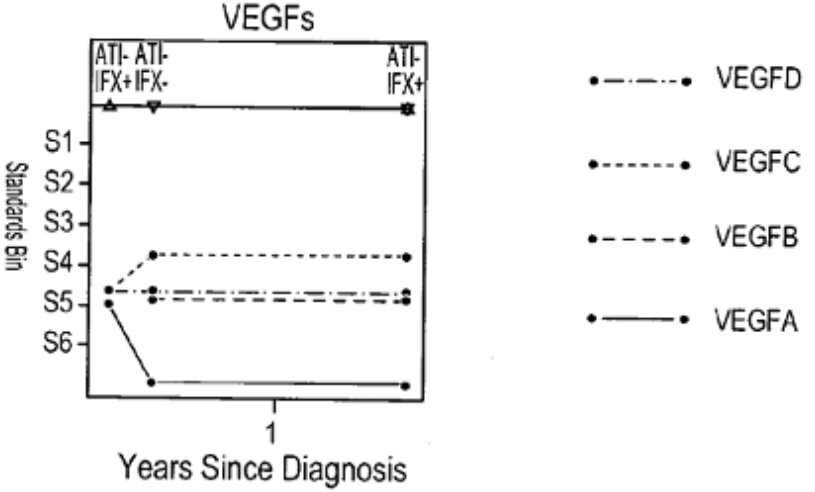
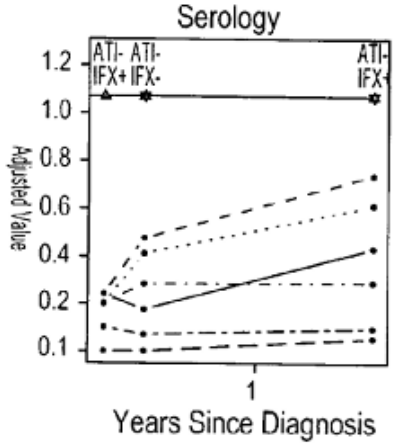


FIG. 8D

Patient #1

FIG. 9A



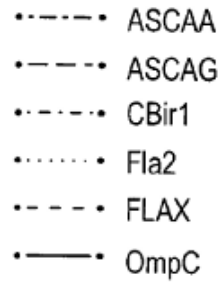
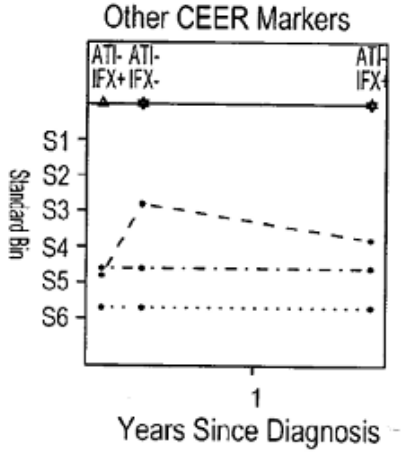
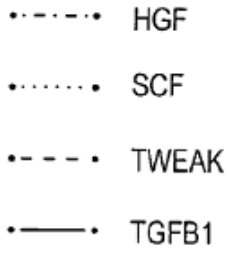
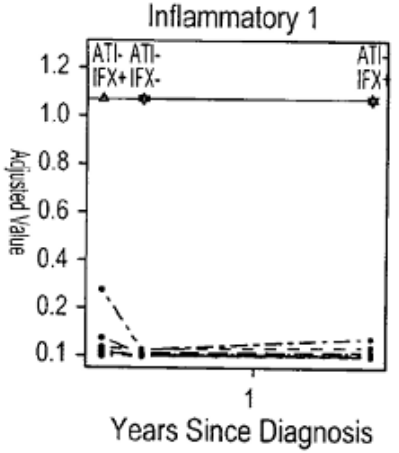


FIG. 9B







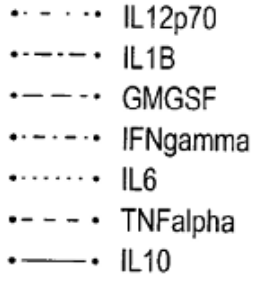
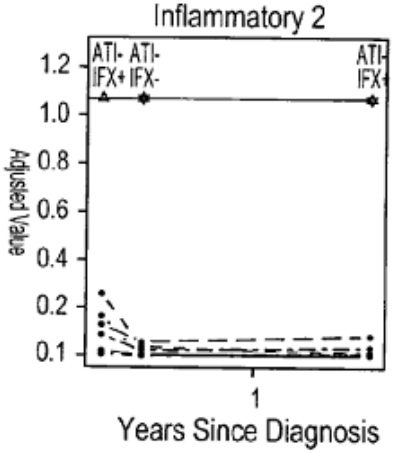


FIG. 9C



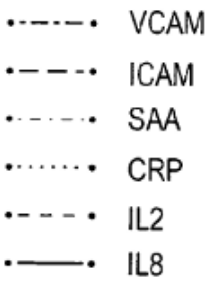


FIG. 9D

Patient #2

FIG. 10A

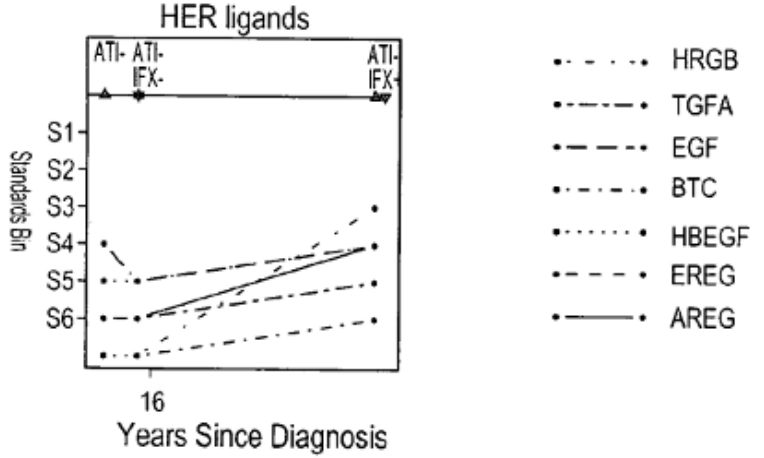


FIG. 10B

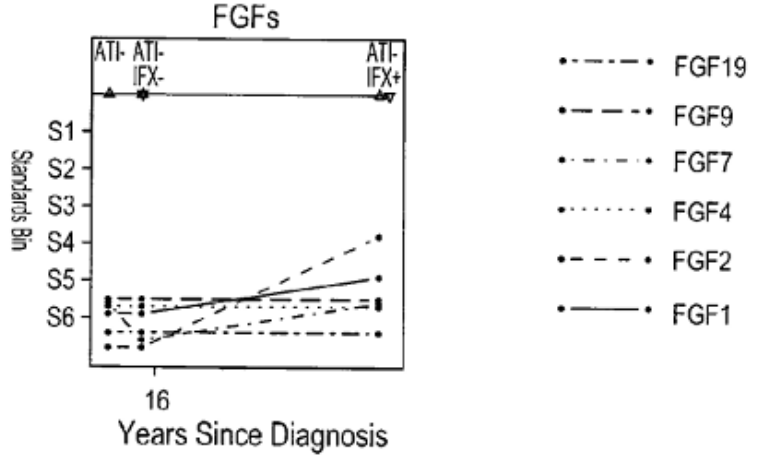


FIG. 10C

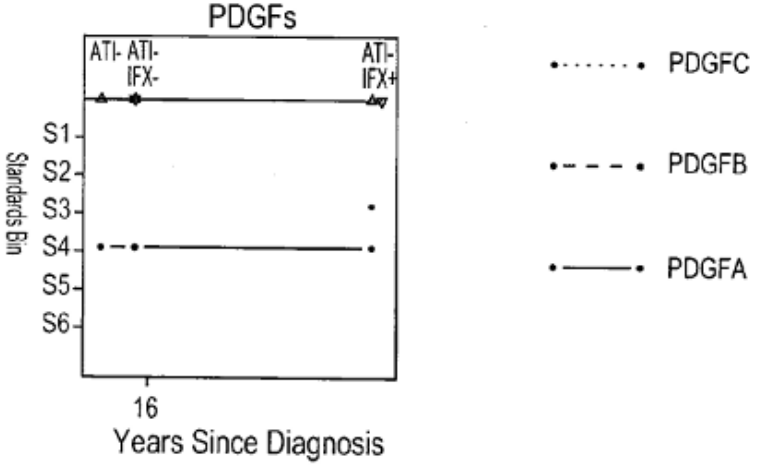
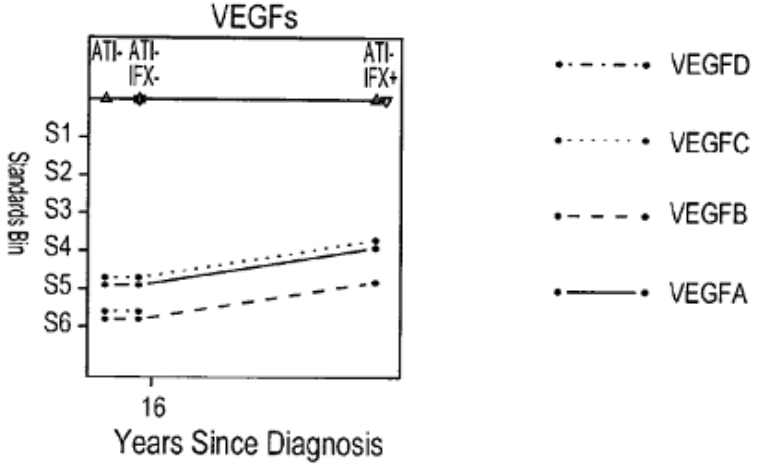
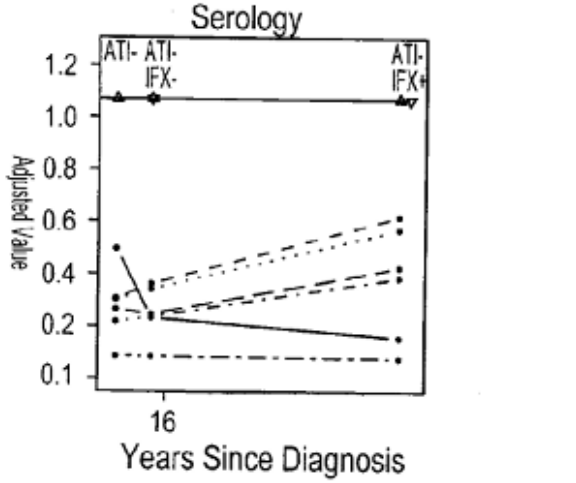


FIG. 10D



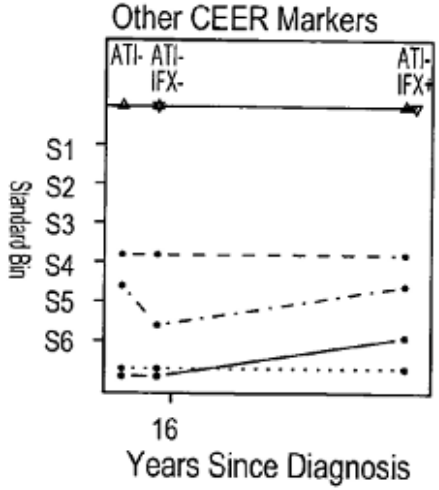
Patient #2

FIG. 11A

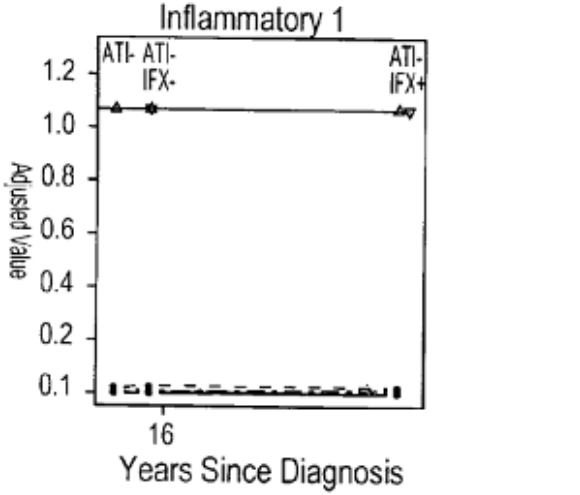


ASCAA
ASCAG
CBir1
Fla2
FLAX
OmpC

FIG. 11B

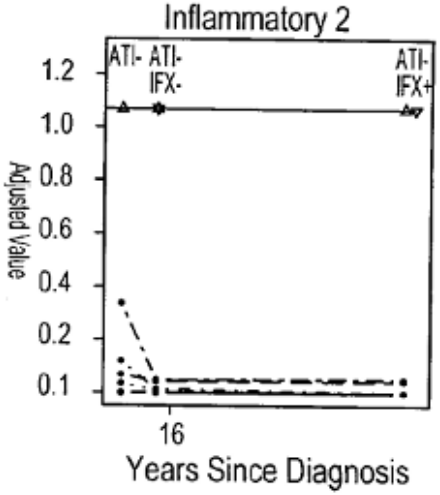


HGF
SCF
TWEAK
TGFB1



IL12p70
IL1B
GMGSF
IFNgamma
IL6
TNFalpha
IL10

FIG. 11C



VCAM
ICAM
SAA
CRP
IL2
IL8

FIG. 11D

Patient #3

FIG. 12A

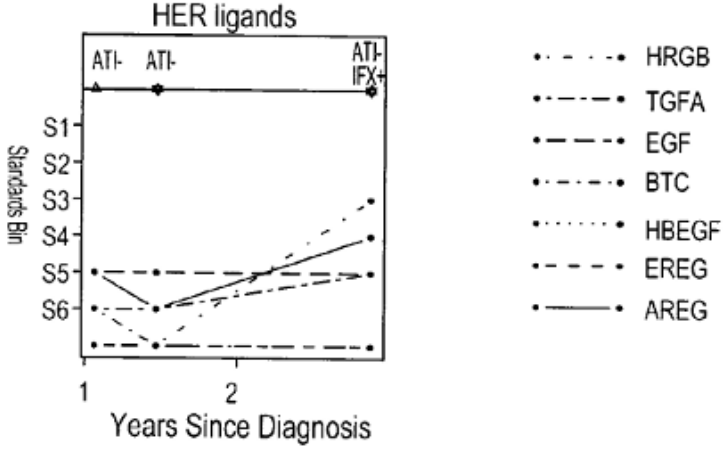
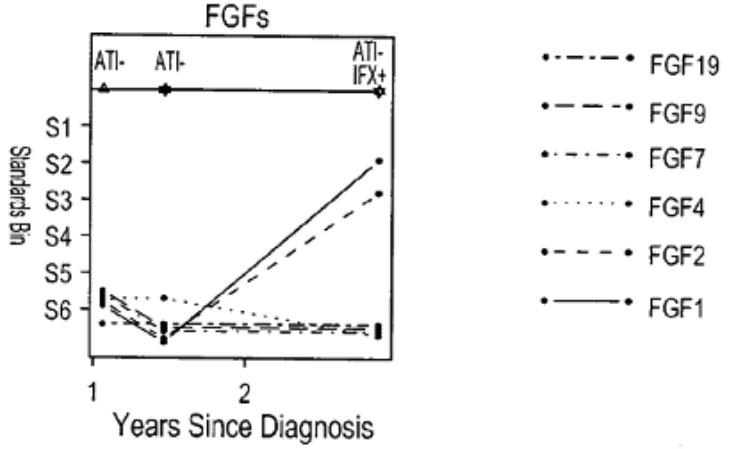


FIG. 12B



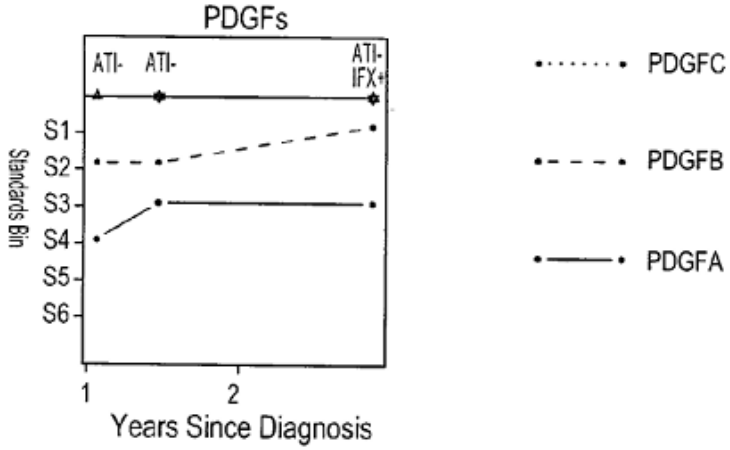


FIG. 12C

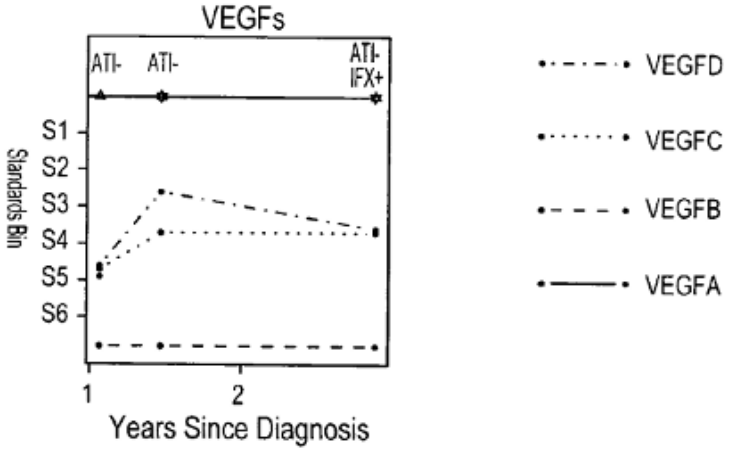
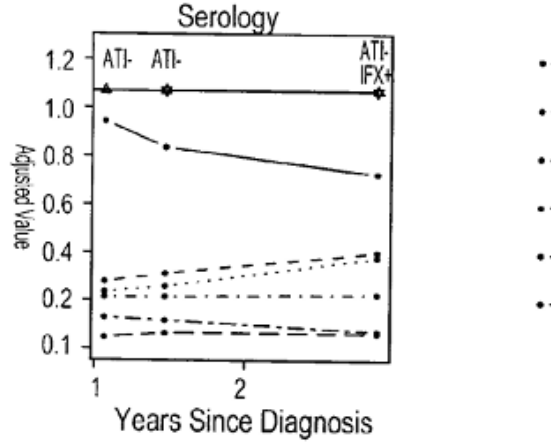


FIG. 12D

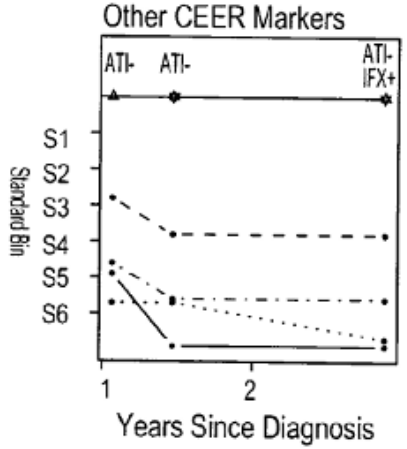
Patient #3

FIG. 13A

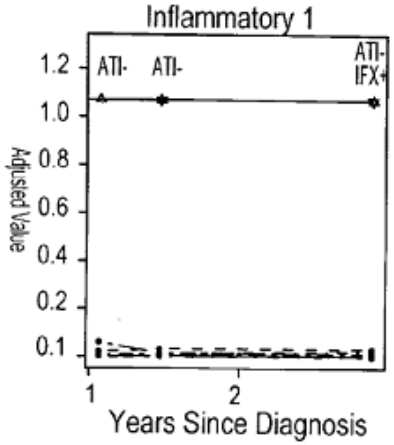


ASCAA
ASCAG
CBir1
Fla2
FLAX
OmpC

FIG. 13B

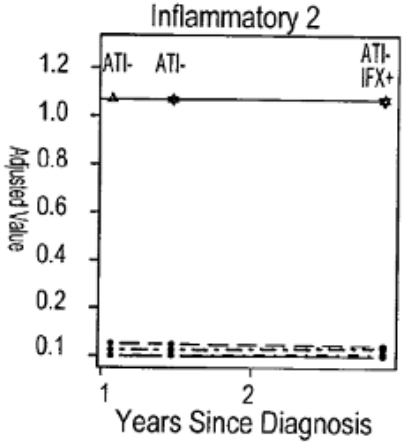


HGF
SCF
TWEAK
TGFB1



IL12p70
IL1B
GMGSF
IFNgamma
IL6
TNFalpha
IL10

FIG. 13C



VCAM
ICAM
SAA
CRP
IL2
IL8

FIG. 13D

Patient #4

FIG. 14A

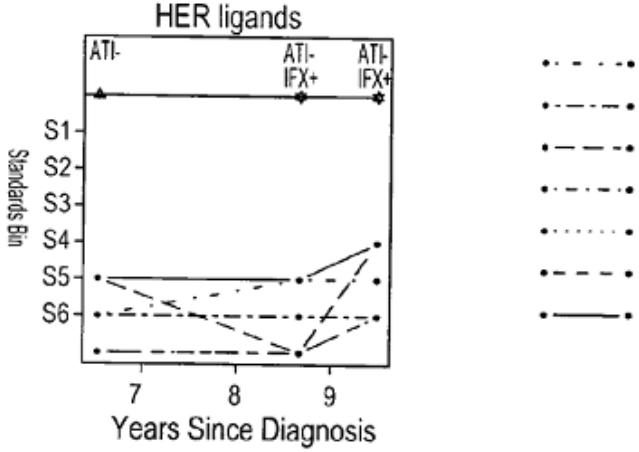
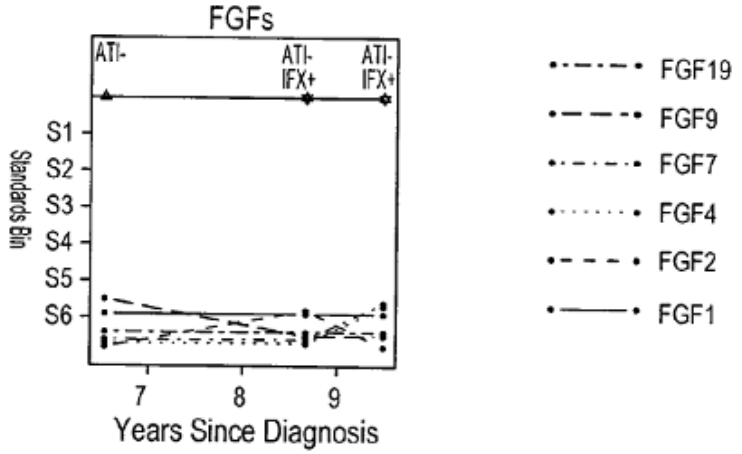


FIG. 14B



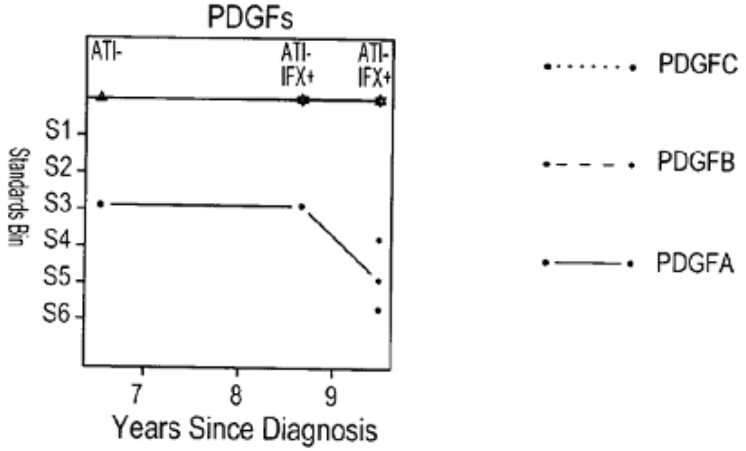


FIG. 14C

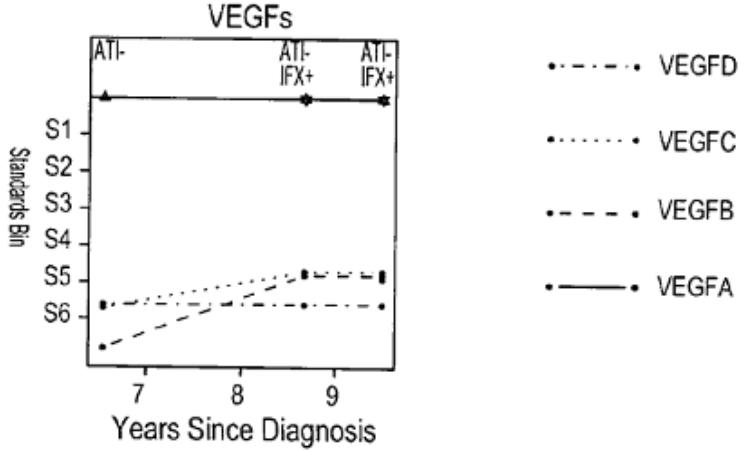
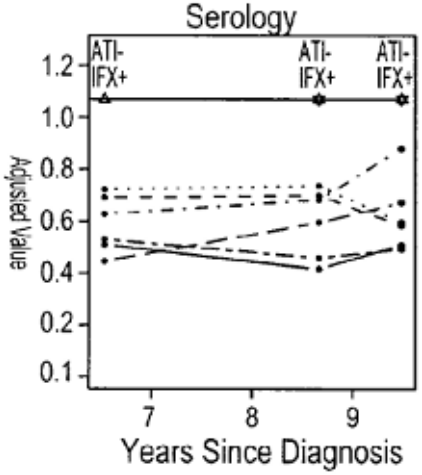


FIG. 14D

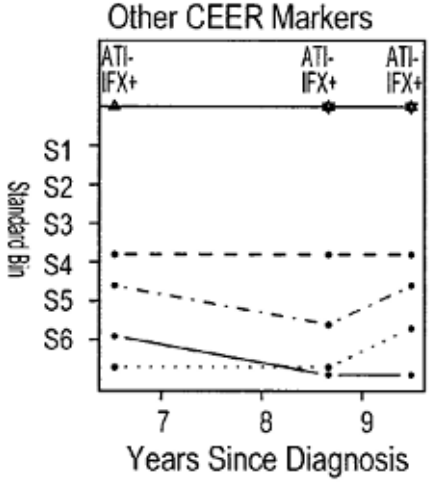
Patient #4

FIG. 15A

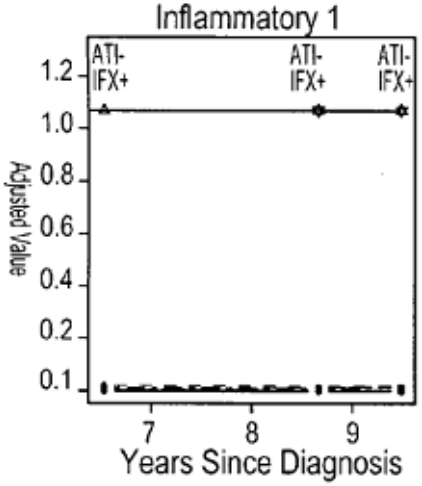


ASCAA
ASCAG
CBir1
Fla2
FLAX
OmpC

FIG. 15B

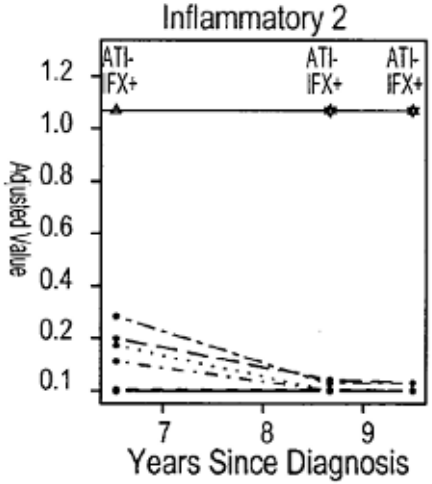


HGF
SCF
TWEAK
TGFB1



IL12p70
IL1B
GMGSF
IFNgamma
IL6
TNFalpha
IL10

FIG. 15C



VCAM
ICAM
SAA
CRP
IL2
IL8

FIG. 15D

Patient #5

FIG. 16A

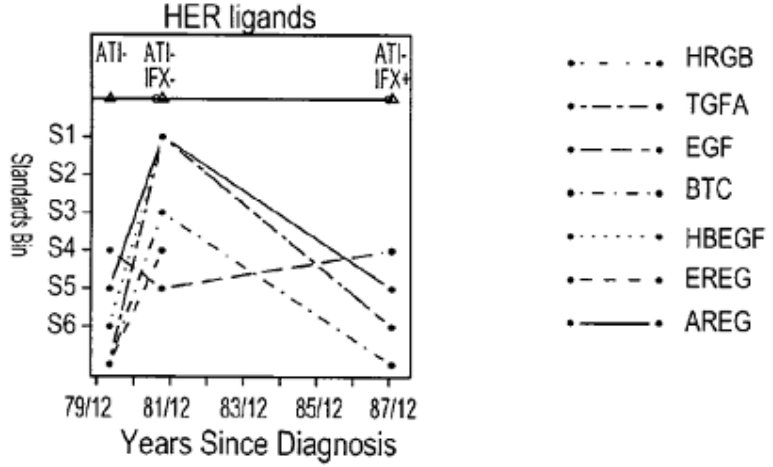
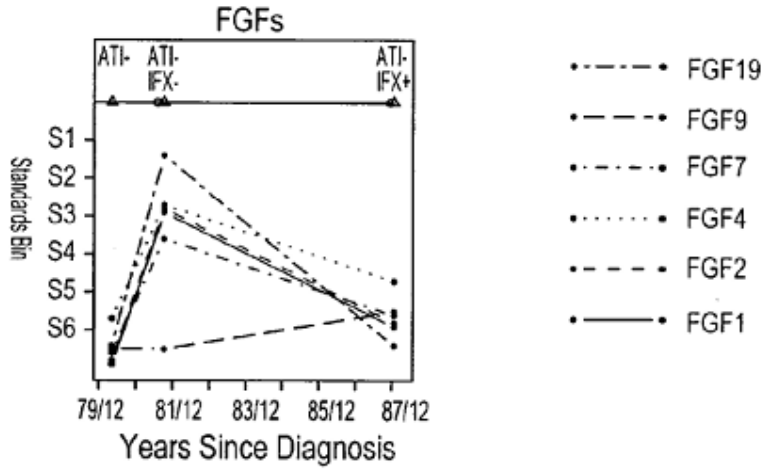


FIG. 16B



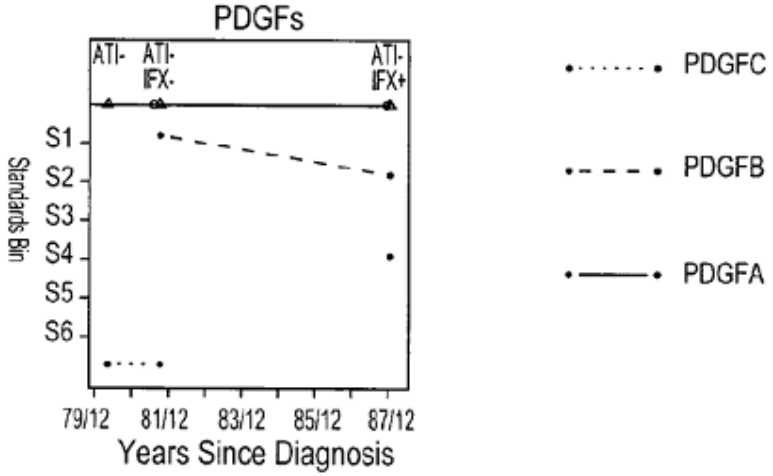


FIG. 16C

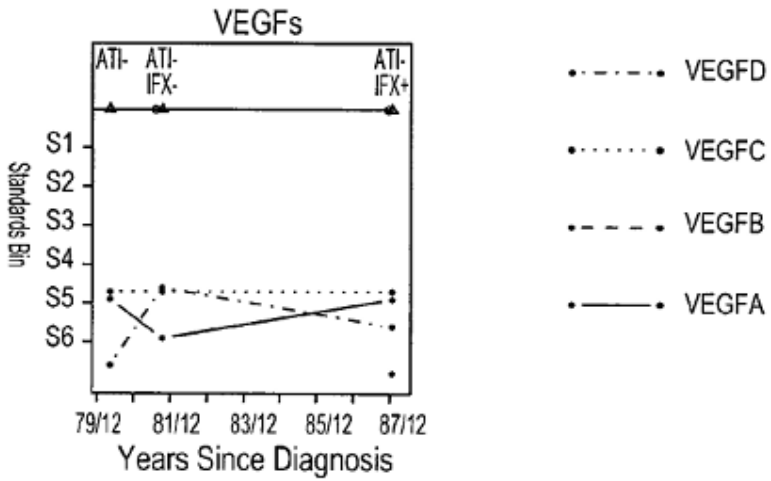
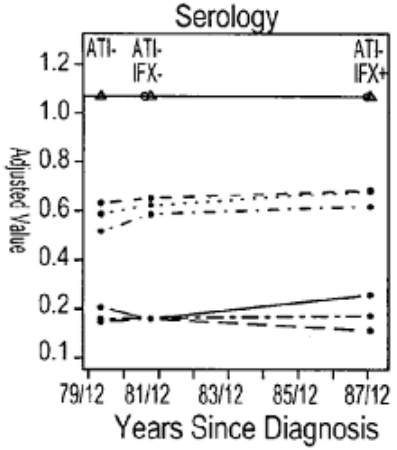


FIG. 16D

Patient #5

FIG. 17A



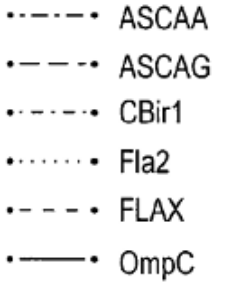
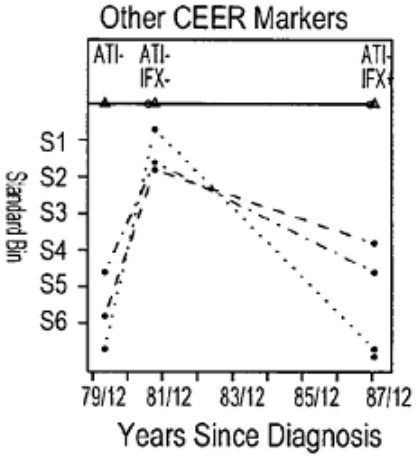
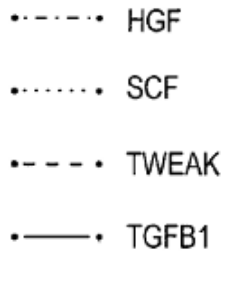
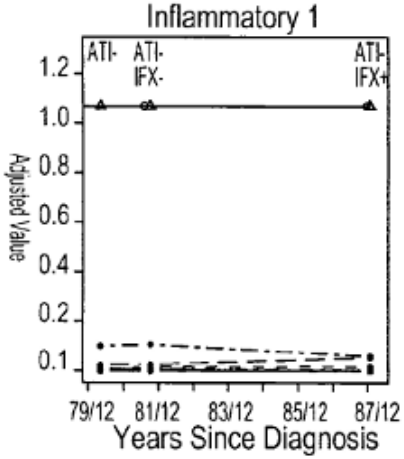


FIG. 17B







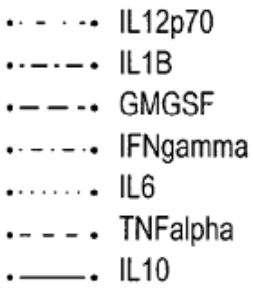
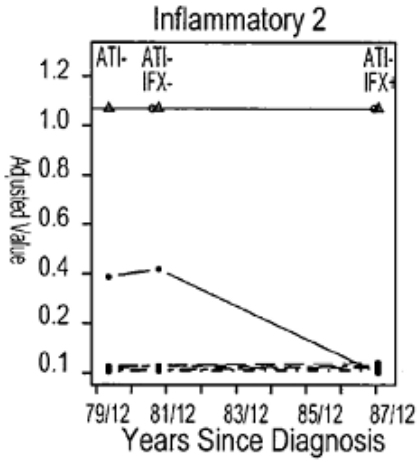


FIG. 17C



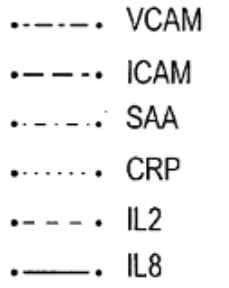


FIG. 17D

Patient #6

FIG. 18A

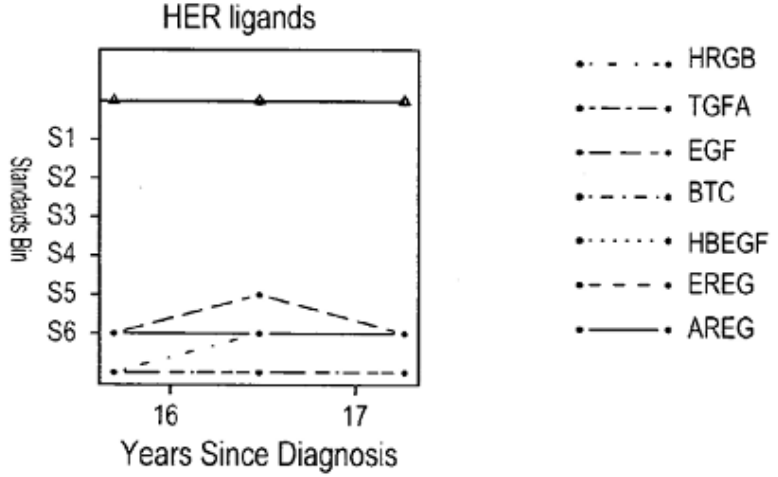
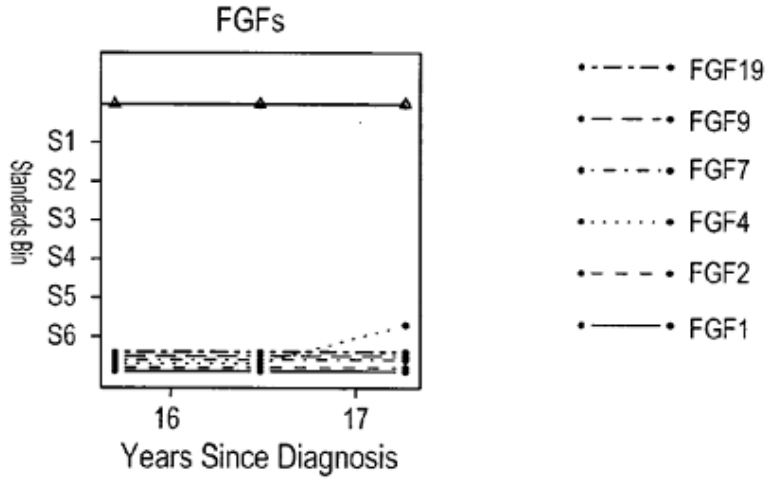


FIG. 18B



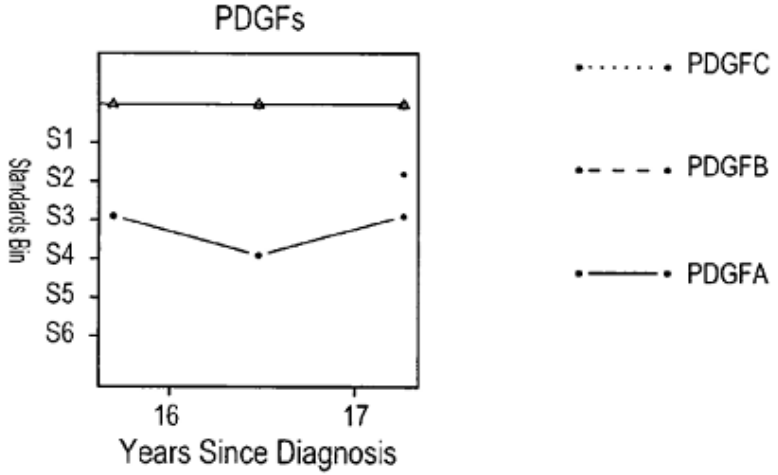


FIG. 18C

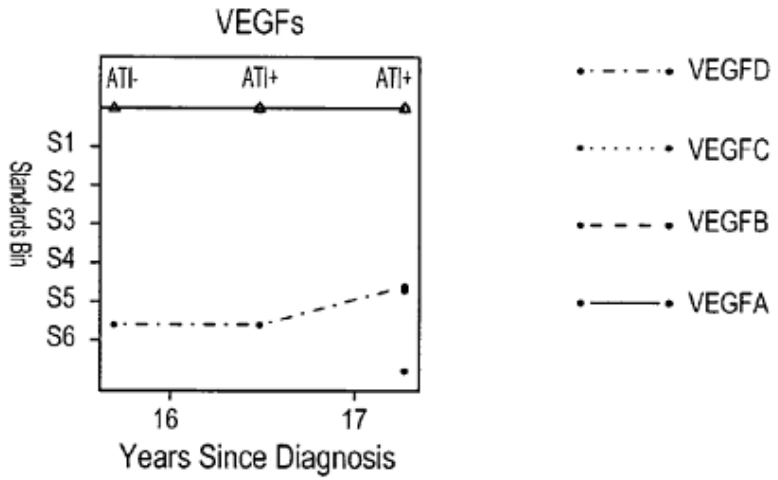
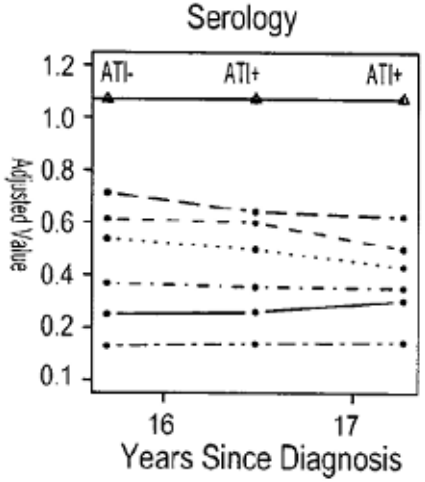


FIG. 18D

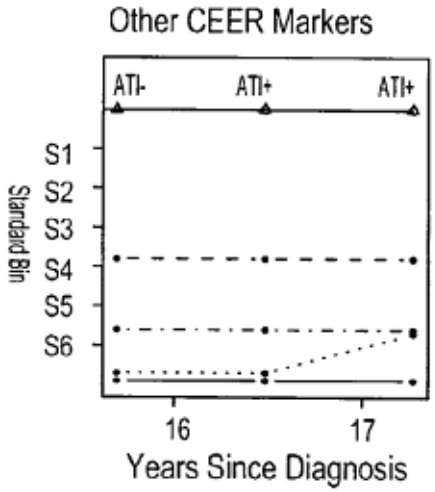
Patient #6

FIG. 19A

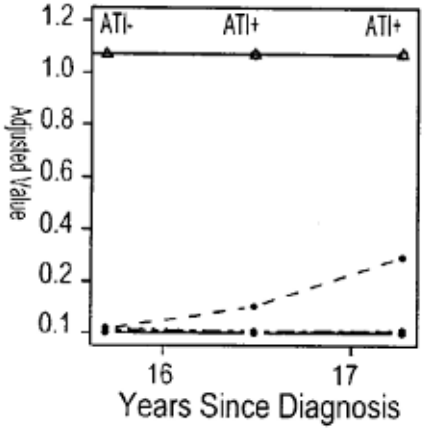


ASCAA
ASCAG
CBir1
Fla2
FLAX
OmpC

FIG. 19B

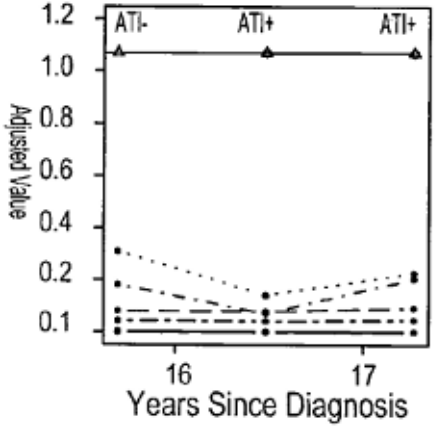


HGF
SCF
TWEAK
TGFB1



IL12p70
IL1B
GMGSF
IFNgamma
IL6
TNFalpha
IL10

FIG. 19C



VCAM
ICAM
SAA
CRP
IL2
IL8

FIG. 19D

Patient #7

FIG. 20A

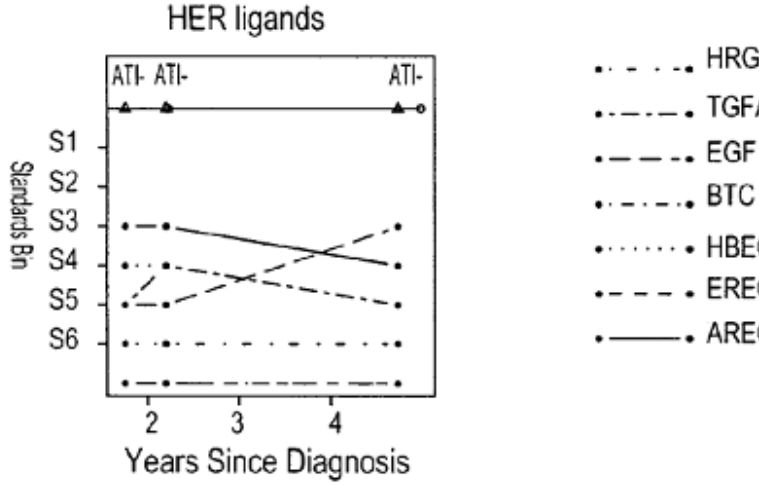


FIG. 20B

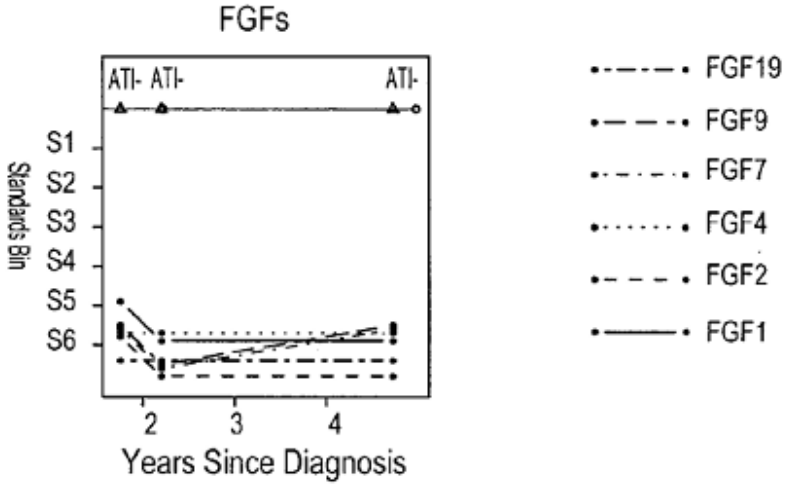


FIG. 20C

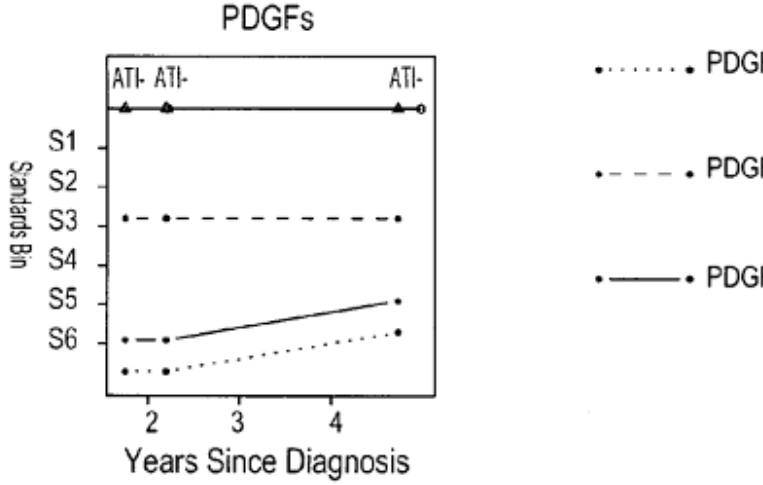
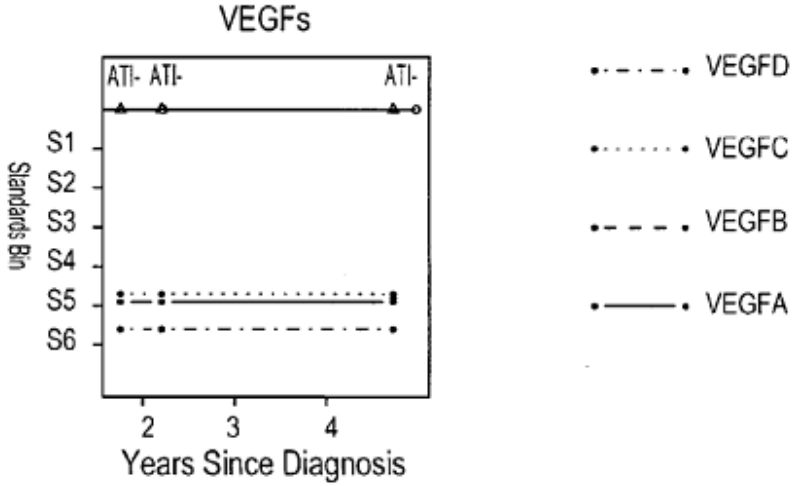


FIG. 20D



Patient #7

FIG. 21A

Serology

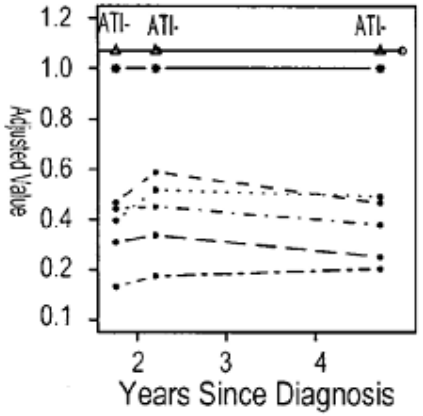
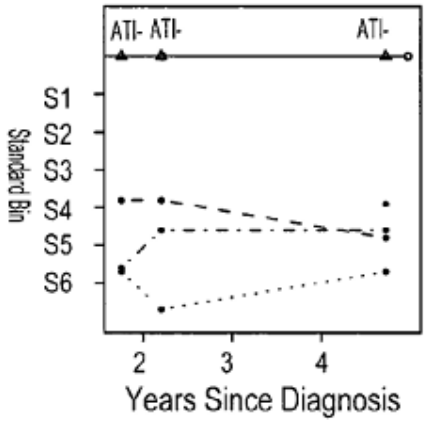
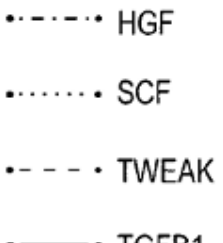




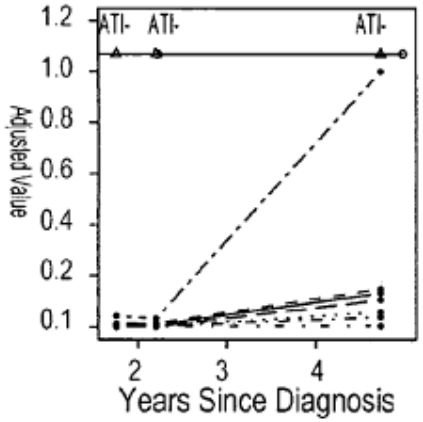
FIG. 21B

Other CEER Markers





Inflammatory 1



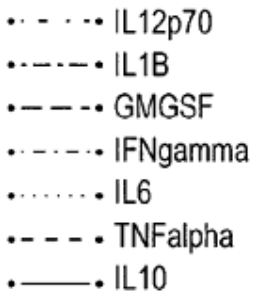
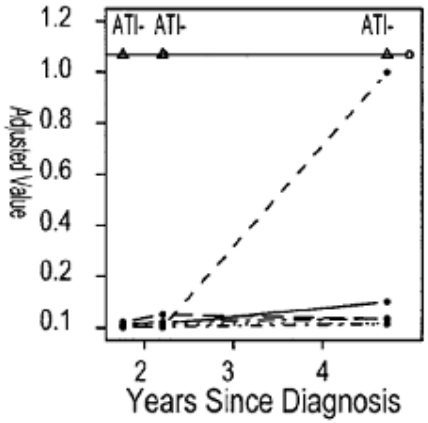


FIG. 21C

Inflammatory 2



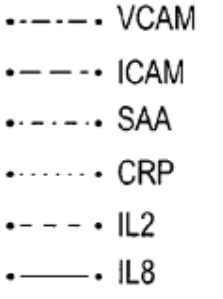


FIG. 21D

Patient #8

FIG. 22A

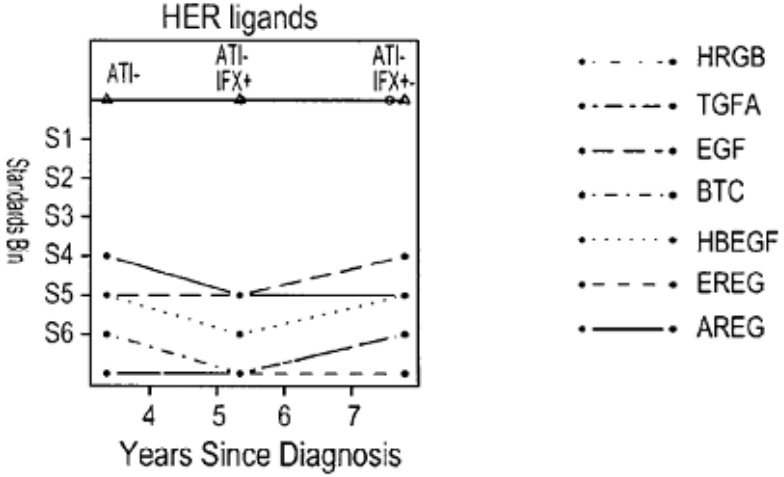
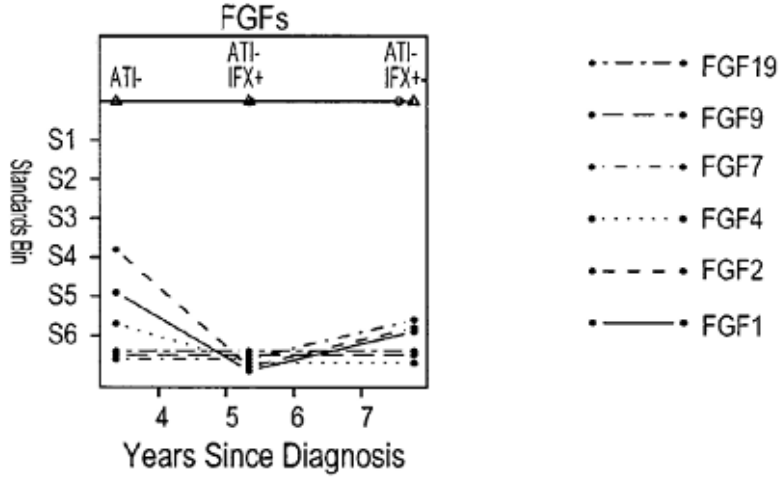


FIG. 22B



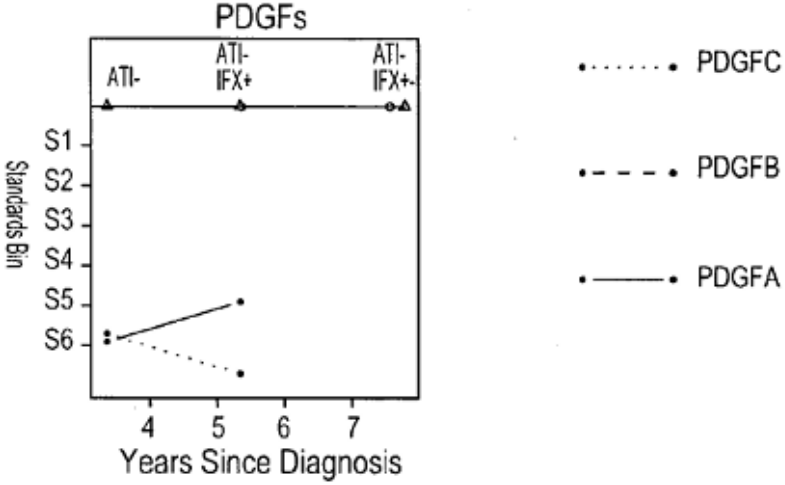


FIG. 22C

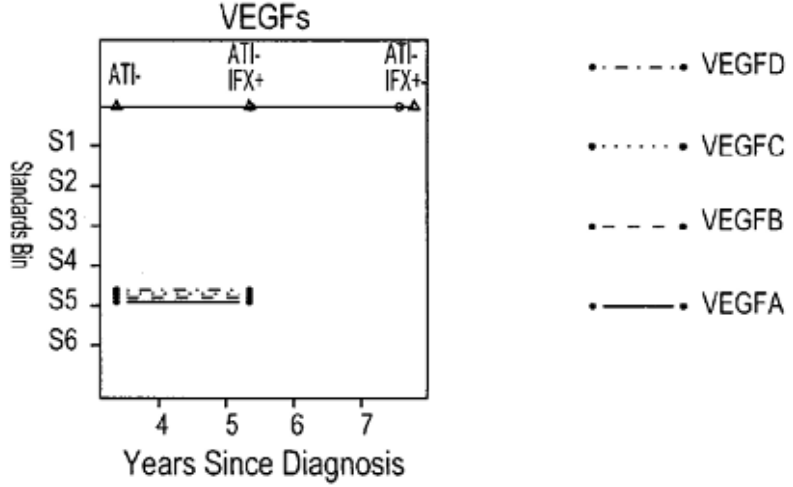
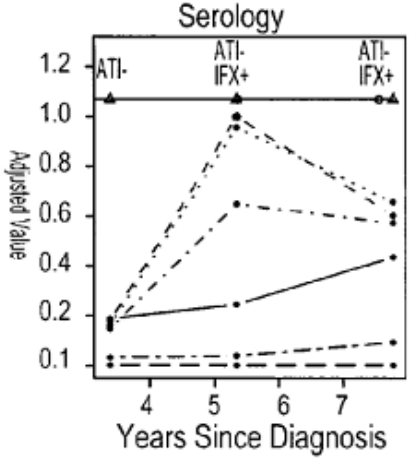


FIG. 22D

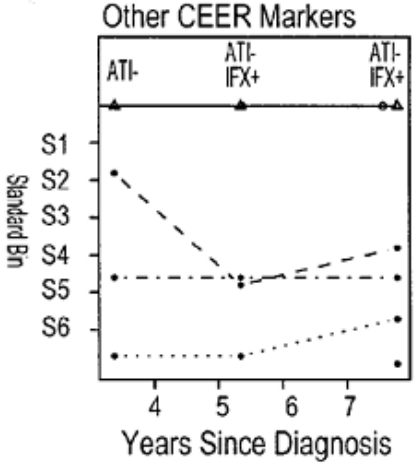
Patient #8

FIG. 23A

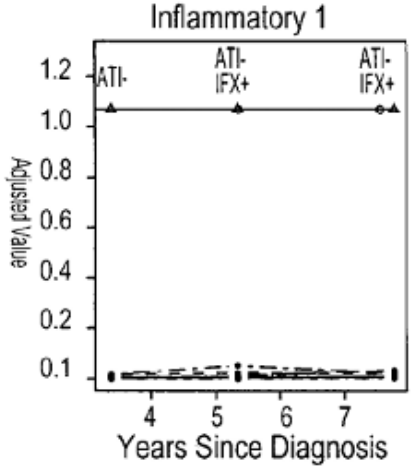


ASCAA
ASCAG
CBir1
Fla2
FLAX
OmpC

FIG. 23B

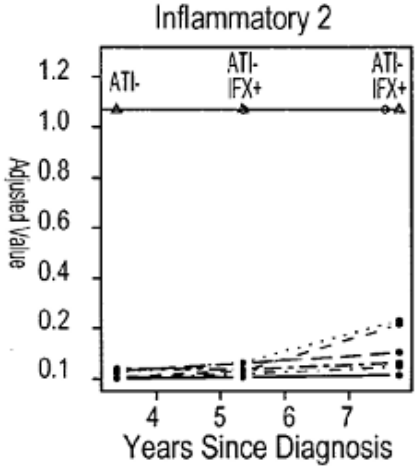


HGF
SCF
TWEAK
TGFB1



IL12p70
IL1B
GMGSF
IFNgamma
IL6
TNFalpha
IL10

FIG. 23C



VCAM
ICAM
SAA
CRP
IL2
IL8

FIG. 23D

FIG. 24A

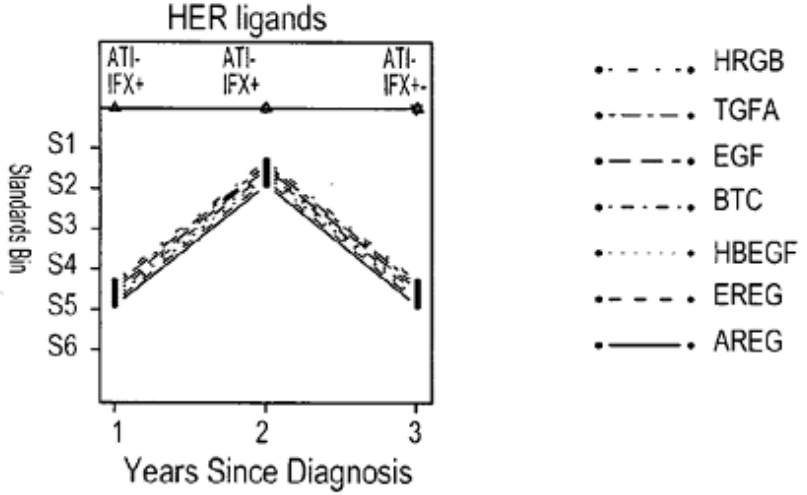
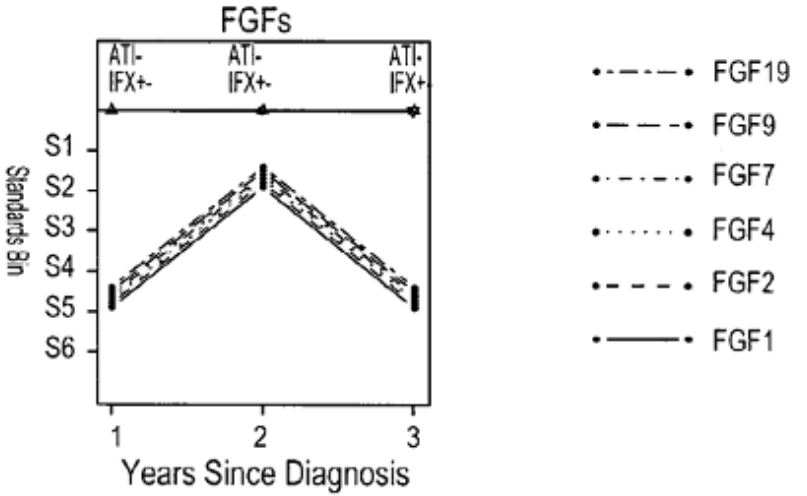


FIG. 24B



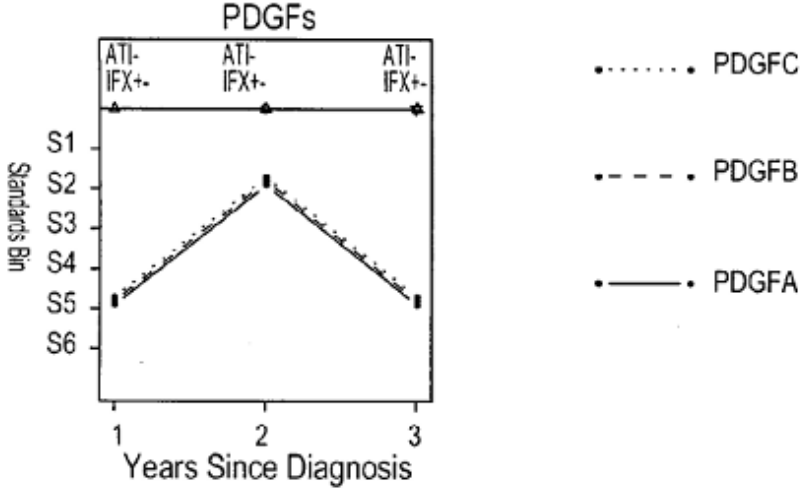


FIG. 24C

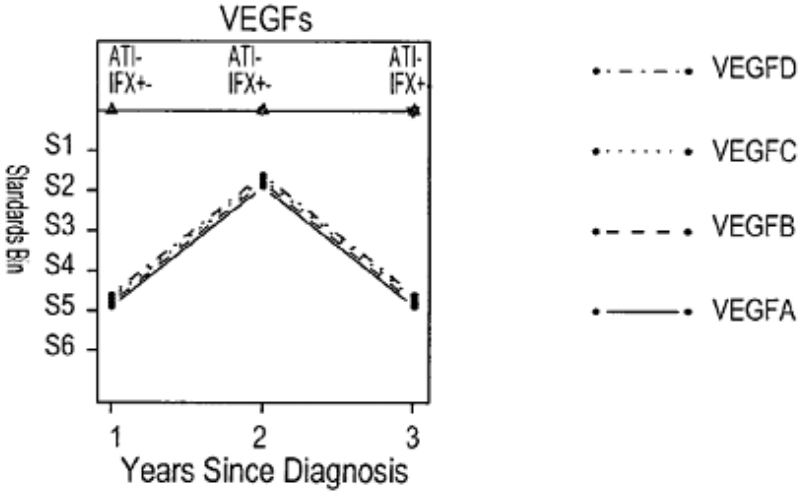
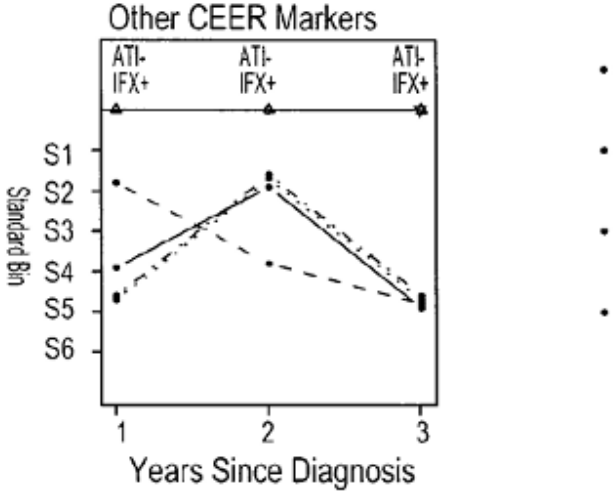
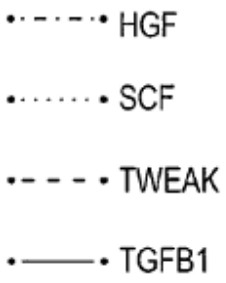
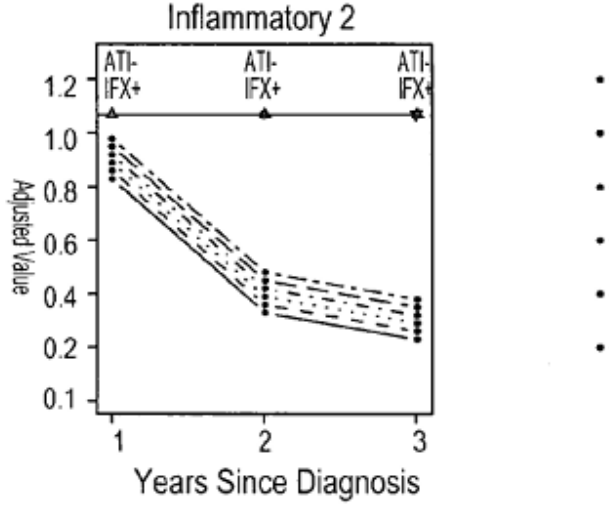


FIG. 24D

FIG. 25A







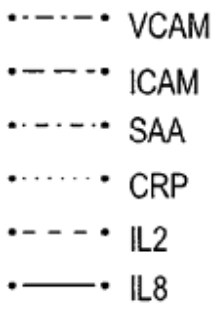
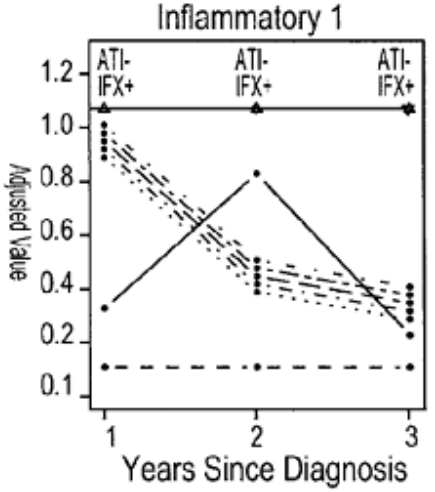
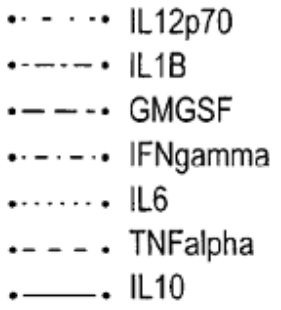


FIG. 25C

FIG. 25B





As patient goes from inflammatory phase (year 1) to proliferation phase (year 2), inflammatory markers go down, even though the patient is not fully healed. Repair factors shown here (HGF, SCF) and anti-inflammatory markers (TGFB1, IL10) go up as patient goes from inflammatory phase to proliferation phase. In remodeling phase (year 3), repair factors and anti-inflammatory markers go down.

AREG	EREG	HBEGF	HGF	HRGB	BTC	EGF	TGFA
2	29	2	2	9	2	2	2
FGF1	FGF2	FGF4	FGF7	FGF9	FGF19	SCF	PDGFA
2	8	2	9	2	4	2	12
PDGFB	PDGFC	VEGFA	VEGFB	VEGFC	VEGFD	TGFB1	TWEAK
25	68	17	47	11	7	29	2

FIG. 26

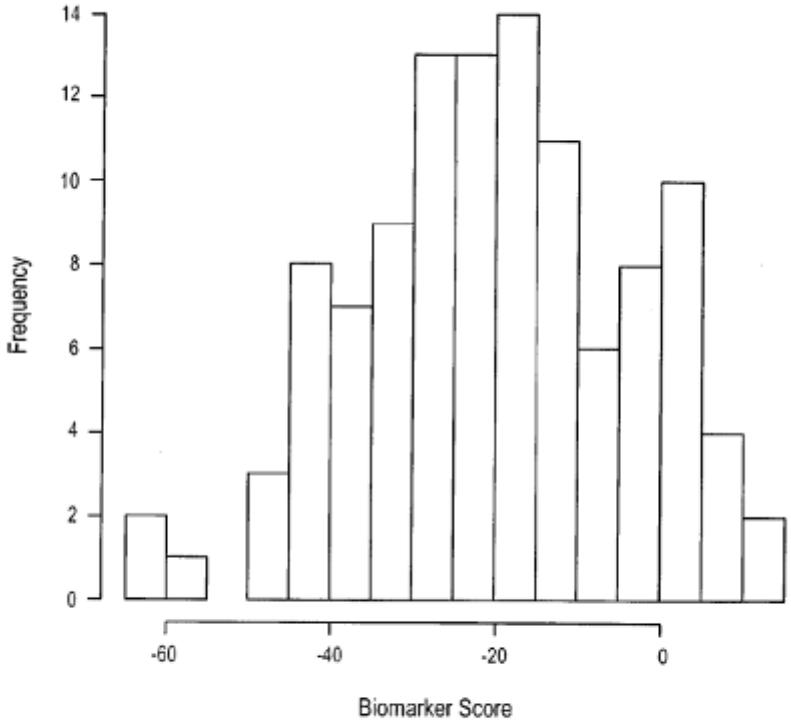


FIG. 27

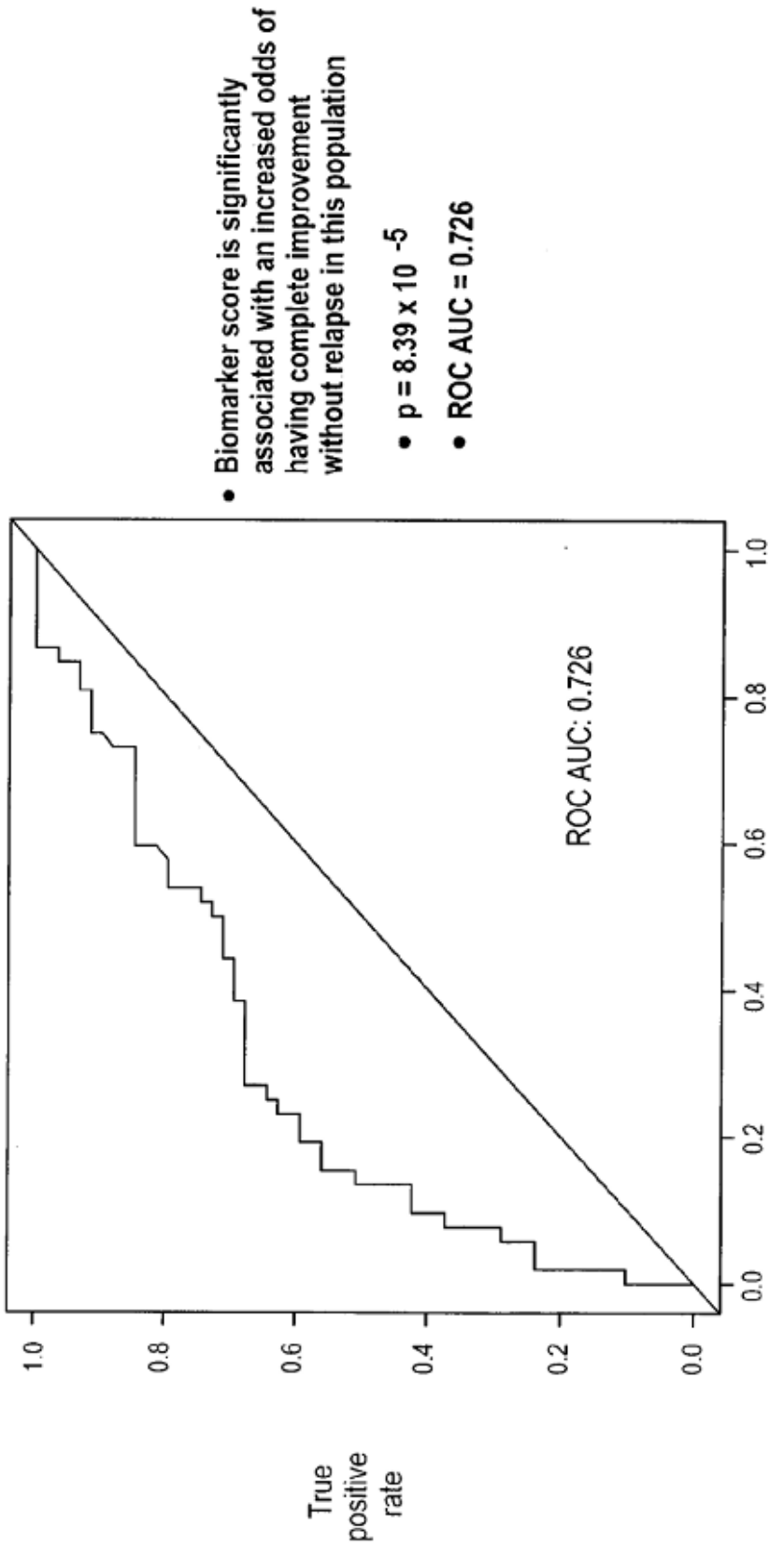

• Biomarker score is significantly associated with an increased odds of having complete improvement without relapse in this population
• p = 8.39 x 10 -5
• ROC AUC = 0.726
ROC AUC: 0.726
True positive rate
False positive rate
0.0
0.2
0.4
0.6
0.8
1.0

FIG. 28

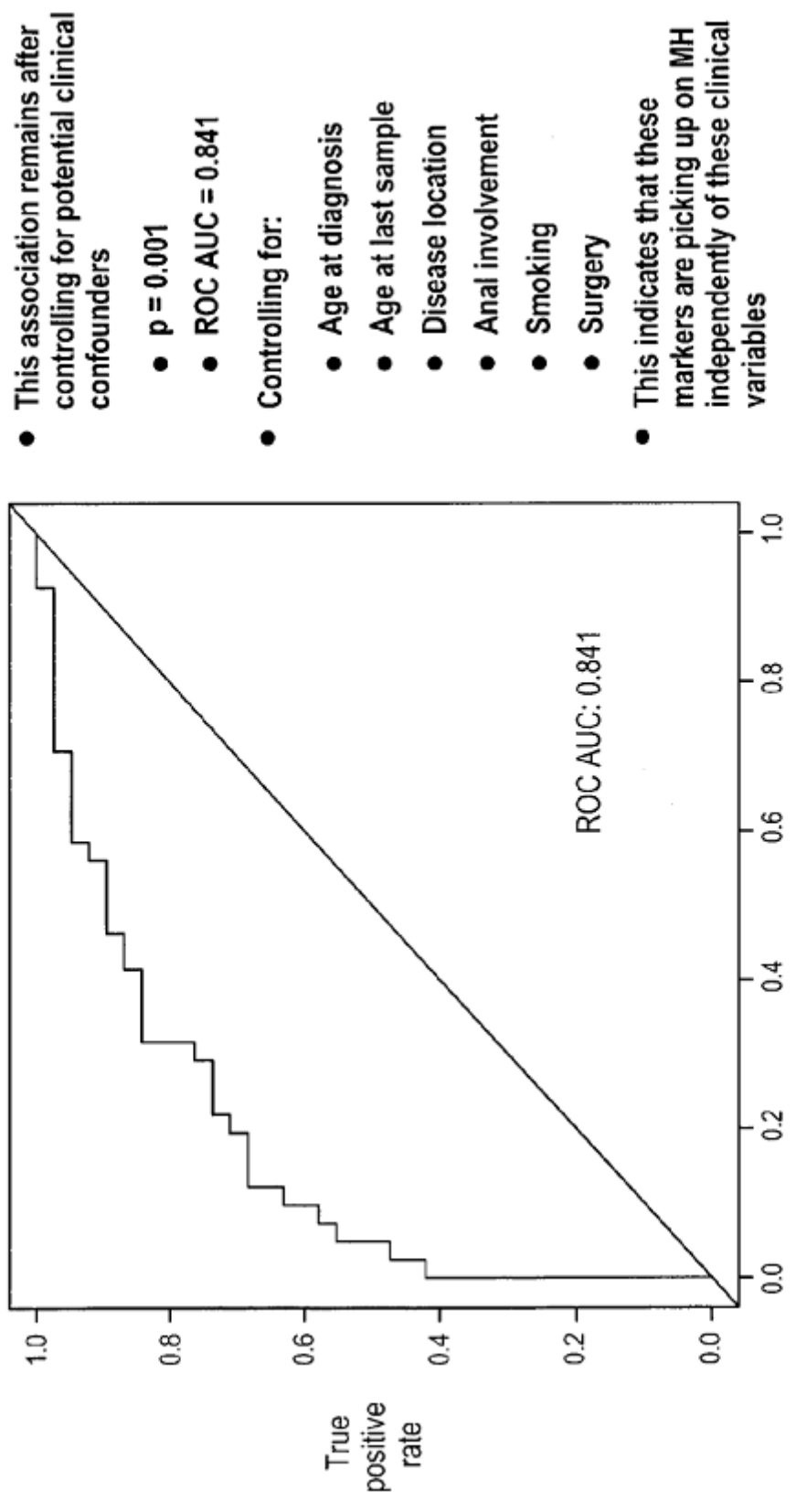

This association remains after controlling for potential clinical confounders
p = 0.001
ROC AUC = 0.841
Controlling for:
Age at diagnosis
Age at last sample
Disease location
Anal involvement
Smoking
Surgery
This indicates that these markers are picking up on MH independently of these clinical variables
ROC AUC: 0.841
True positive rate
False positive rate
0.0
0.2
0.4
0.6
0.8
1.0

FIG. 29

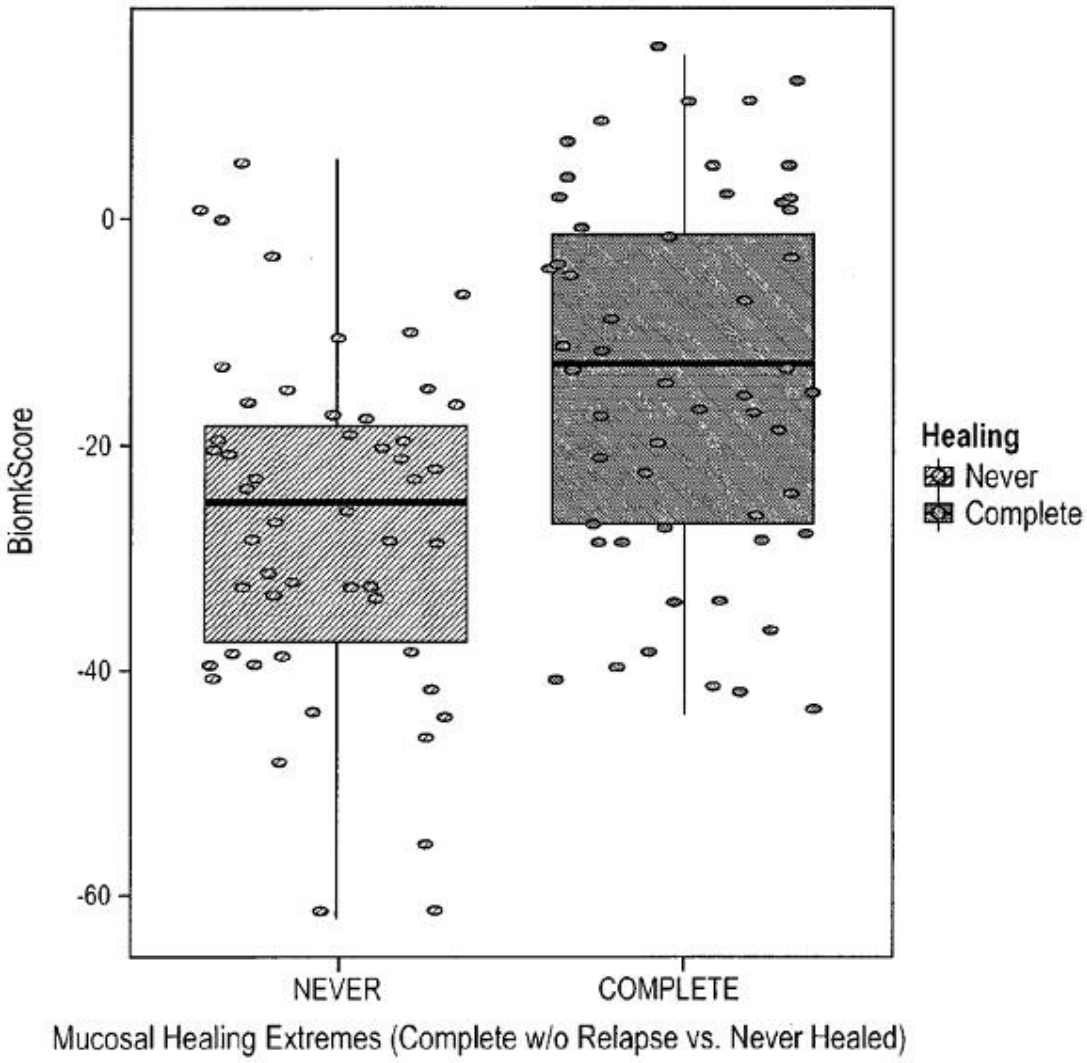

BiomkScore
0
-20
-40
-60
NEVER
COMPLETE
Healing
Never
Complete
Mucosal Healing Extremes (Complete w/o Relapse vs. Never Healed)

FIG. 30

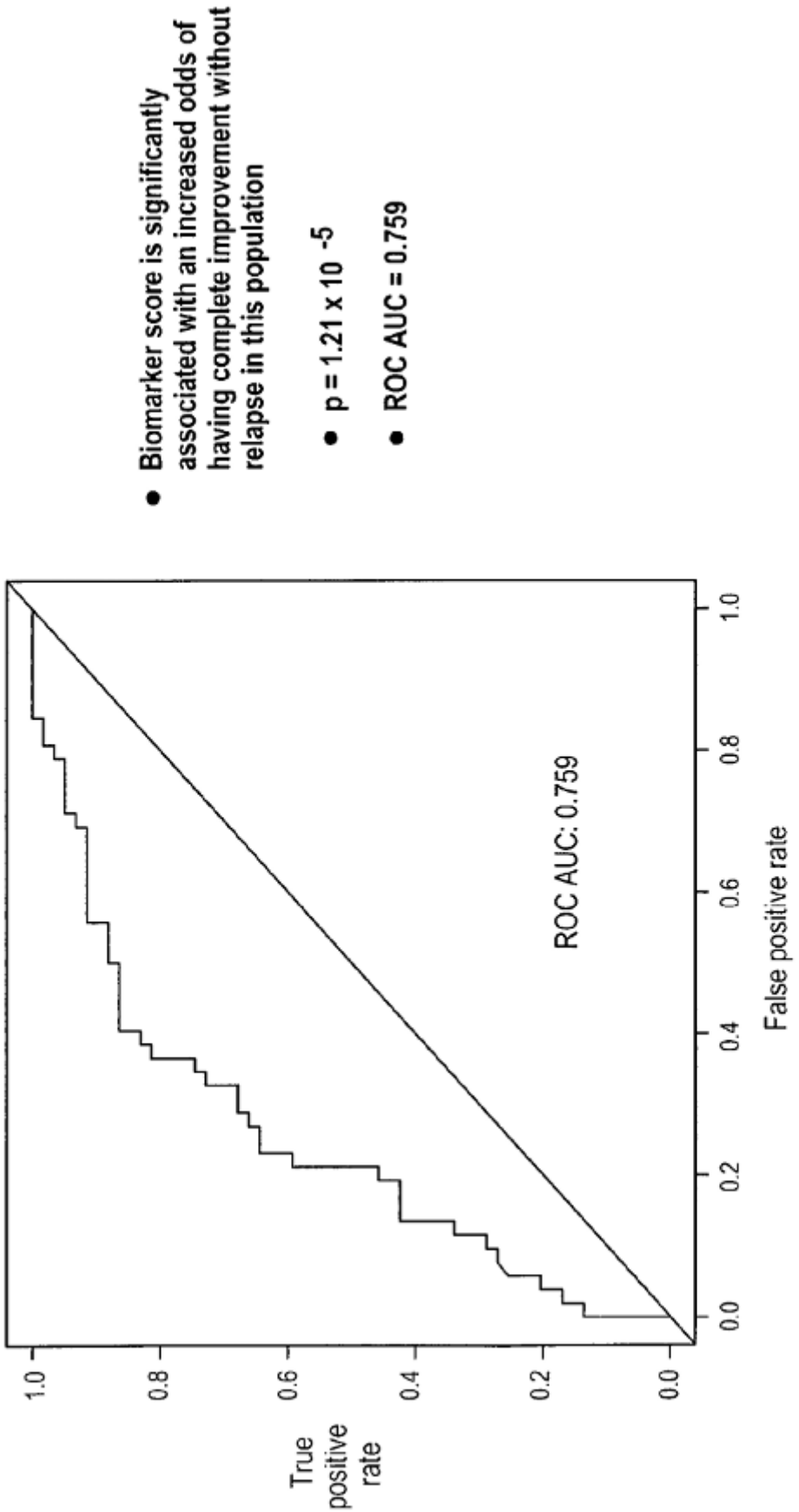
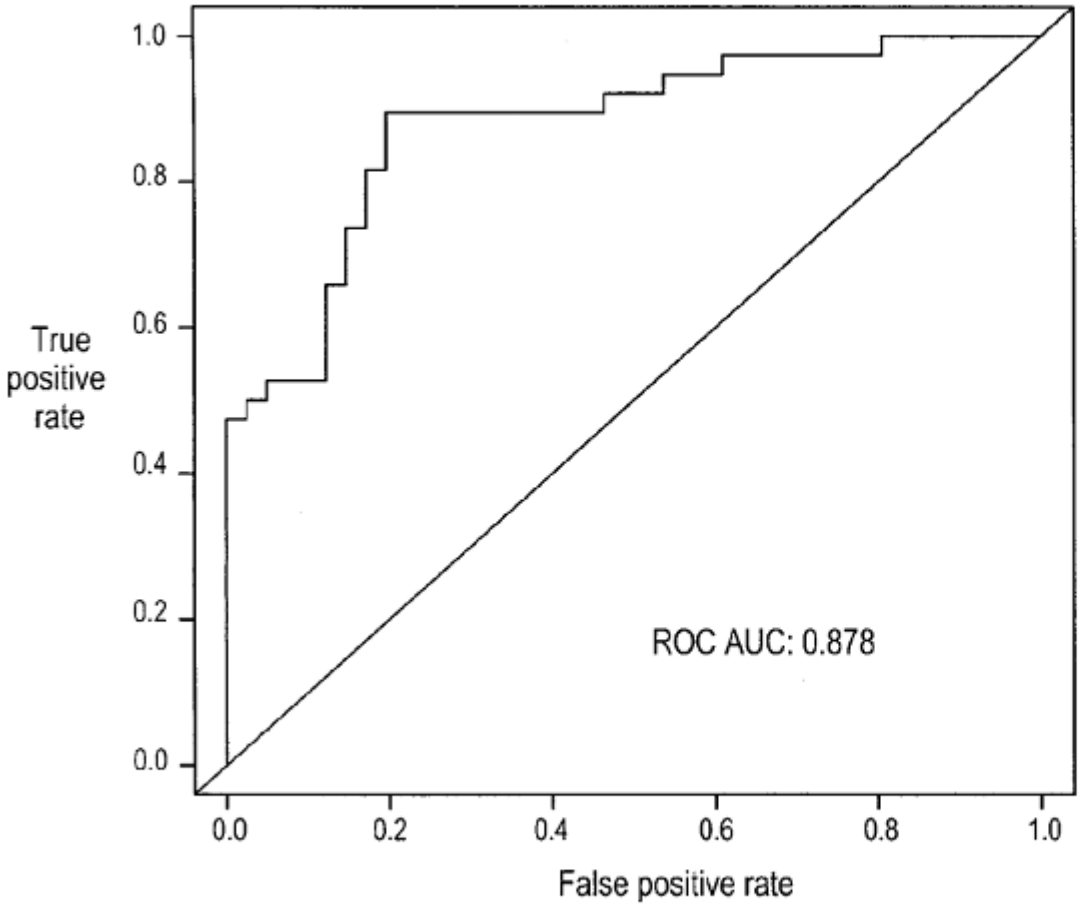

Biomarker score is significantly associated with an increased odds of having complete improvement without relapse in this population
p = 1.21 x 10 -5
ROC AUC = 0.759
ROC AUC: 0.759
True positive rate
False positive rate
0.0
0.2
0.4
0.6
0.8
1.0

FIG. 31



- This association remains after controlling for potential clinical confounders
  - p = 0.0001
  - ROC AUC = 0.878
- Controlling for:
  - Age at diagnosis
  - Age at last sample
  - Disease location
  - Anal involvement
  - Smoking
  - Surgery
- This indicates that these markers are picking up on MH independently of these clinical variables

FIG. 31

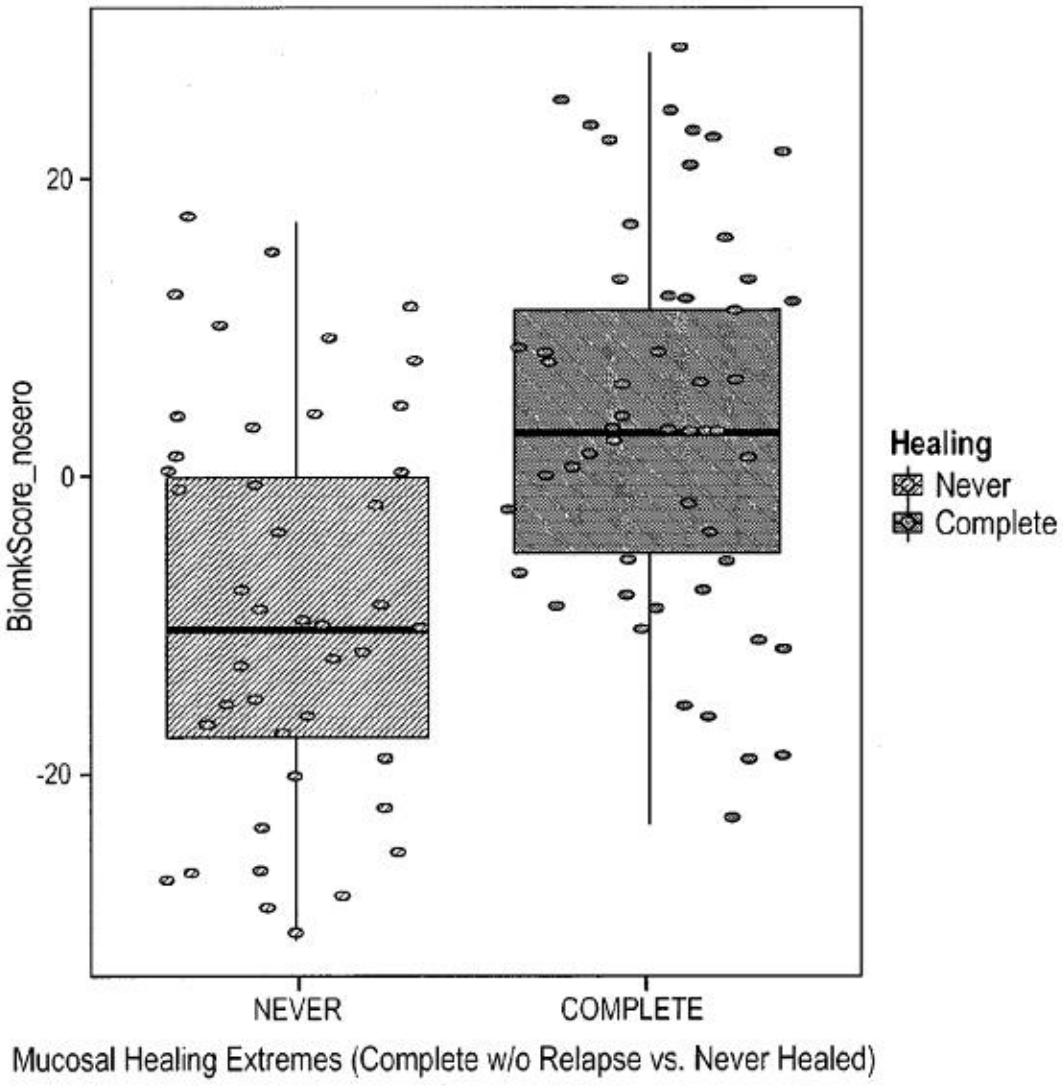

20
0
-20
BiomkScore_nosero
NEVER
COMPLETE
Healing
Never
Complete
Mucosal Healing Extremes (Complete w/o Relapse vs. Never Healed)

FIG. 33

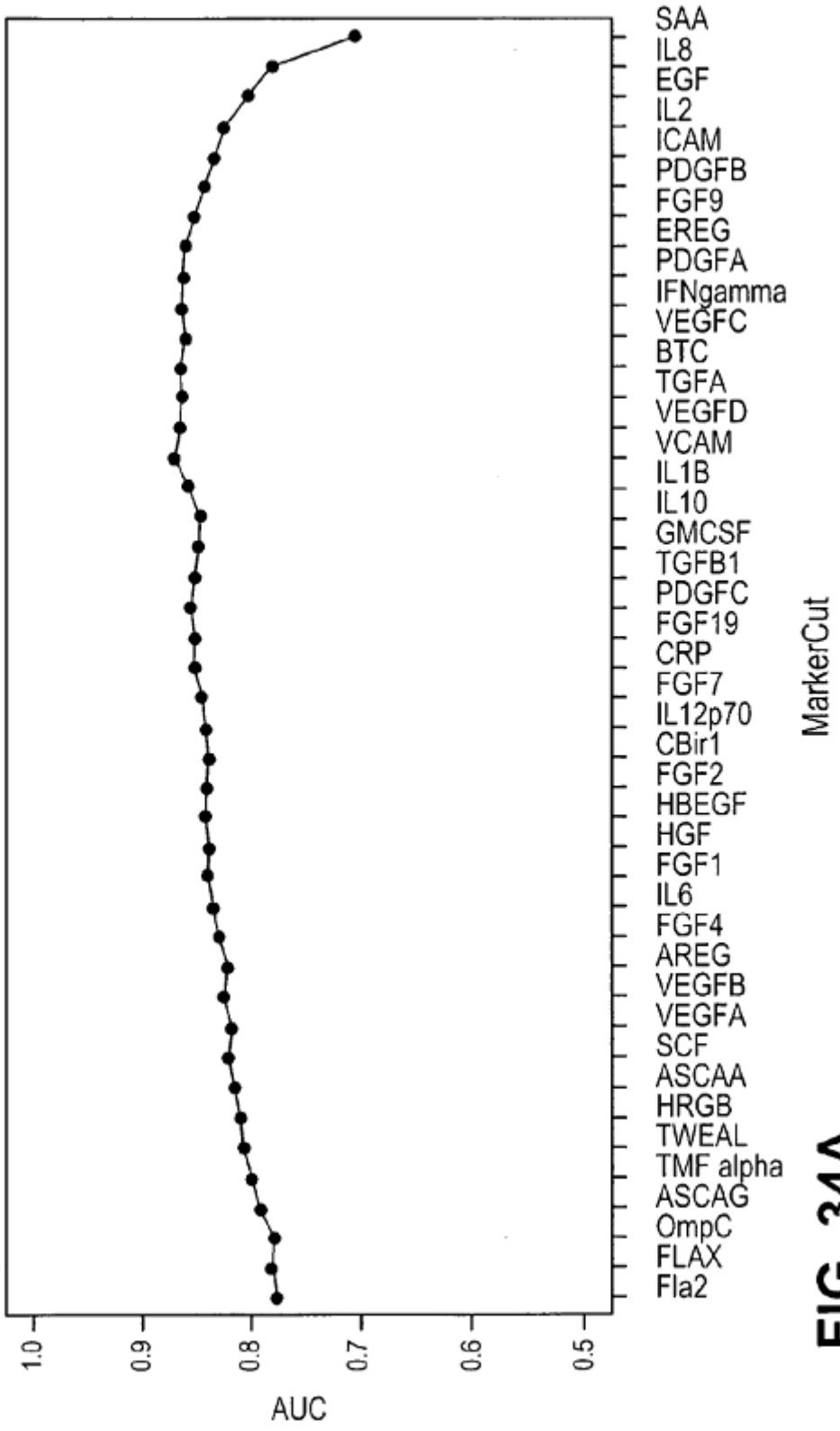

SAA
IL8
EGF
IL2
ICAM
PDGFB
FGF9
EREG
PDGFA
IFNgamma
VEGFC
BTC
TGFA
VEGFD
VCAM
IL1B
IL10
GMCSF
TGFB1
PDGFC
FGF19
CRP
FGF7
IL12p70
CBir1
FGF2
HBEGF
HGF
FGF1
IL6
FGF4
AREG
VEGFB
VEGFA
SCF
ASCAA
HRGB
TWEAL
TMF alpha
ASCAG
OmpC
FLAX
Fla2
MarkerCut
1.0
0.9
0.8
0.7
0.6
0.5
AUC

FIG. 34A

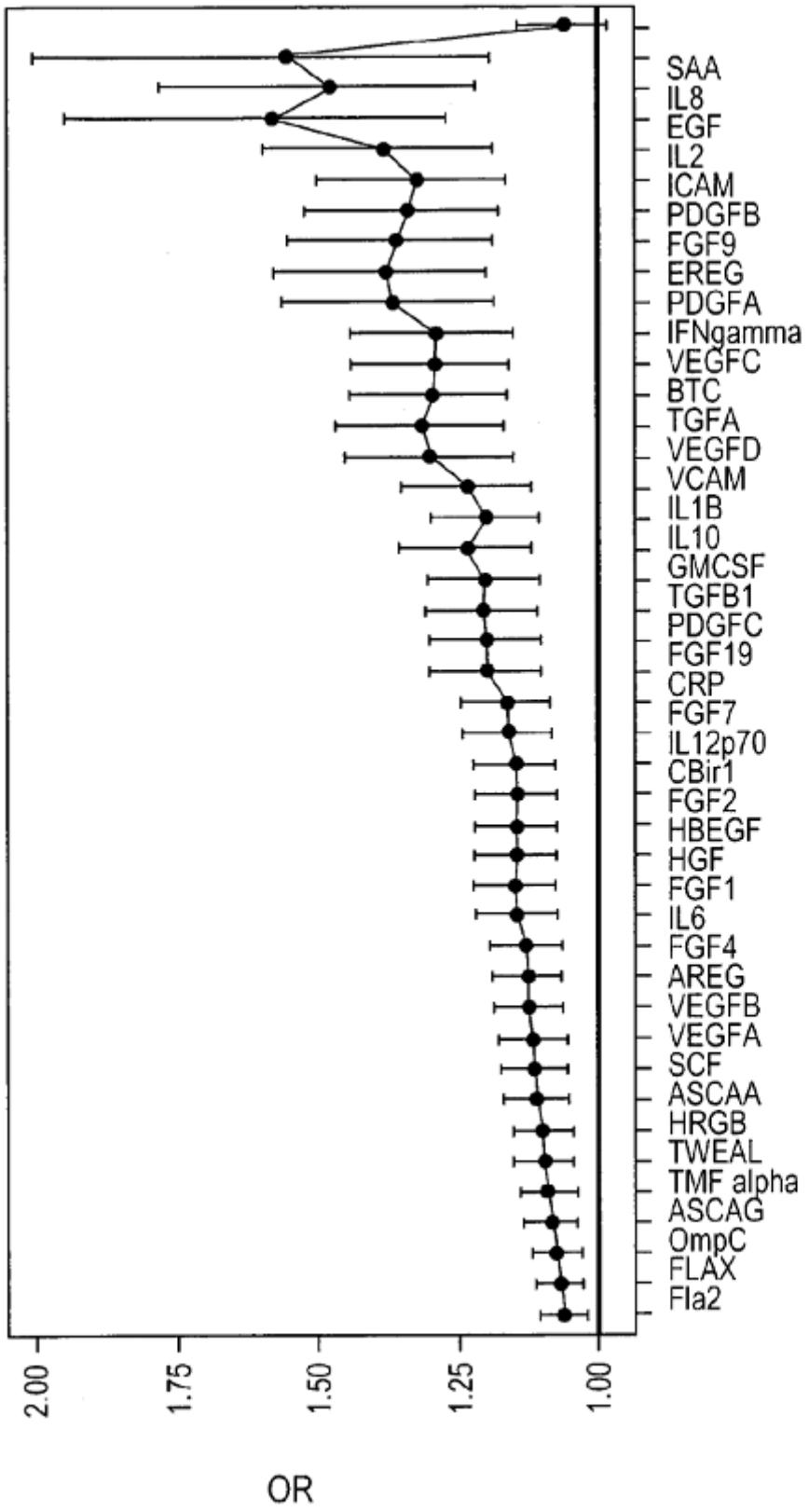

SAA
IL8
EGF
IL2
ICAM
PDGFB
FGF9
EREG
PDGFA
IFNgamma
VEGFC
BTC
TGFA
VEGFD
VCAM
IL1B
IL10
GMCSF
TGFB1
PDGFC
FGF19
CRP
FGF7
IL12p70
CBir1
FGF2
HBEGF
HGF
FGF1
IL6
FGF4
AREG
VEGFB
VEGFA
SCF
ASCAA
HRGB
TWEAL
TMF alpha
ASCAG
OmpC
FLAX
Fla2
MarkerCut
2.00
1.75
1.50
1.25
1.00
OR

FIG. 34B

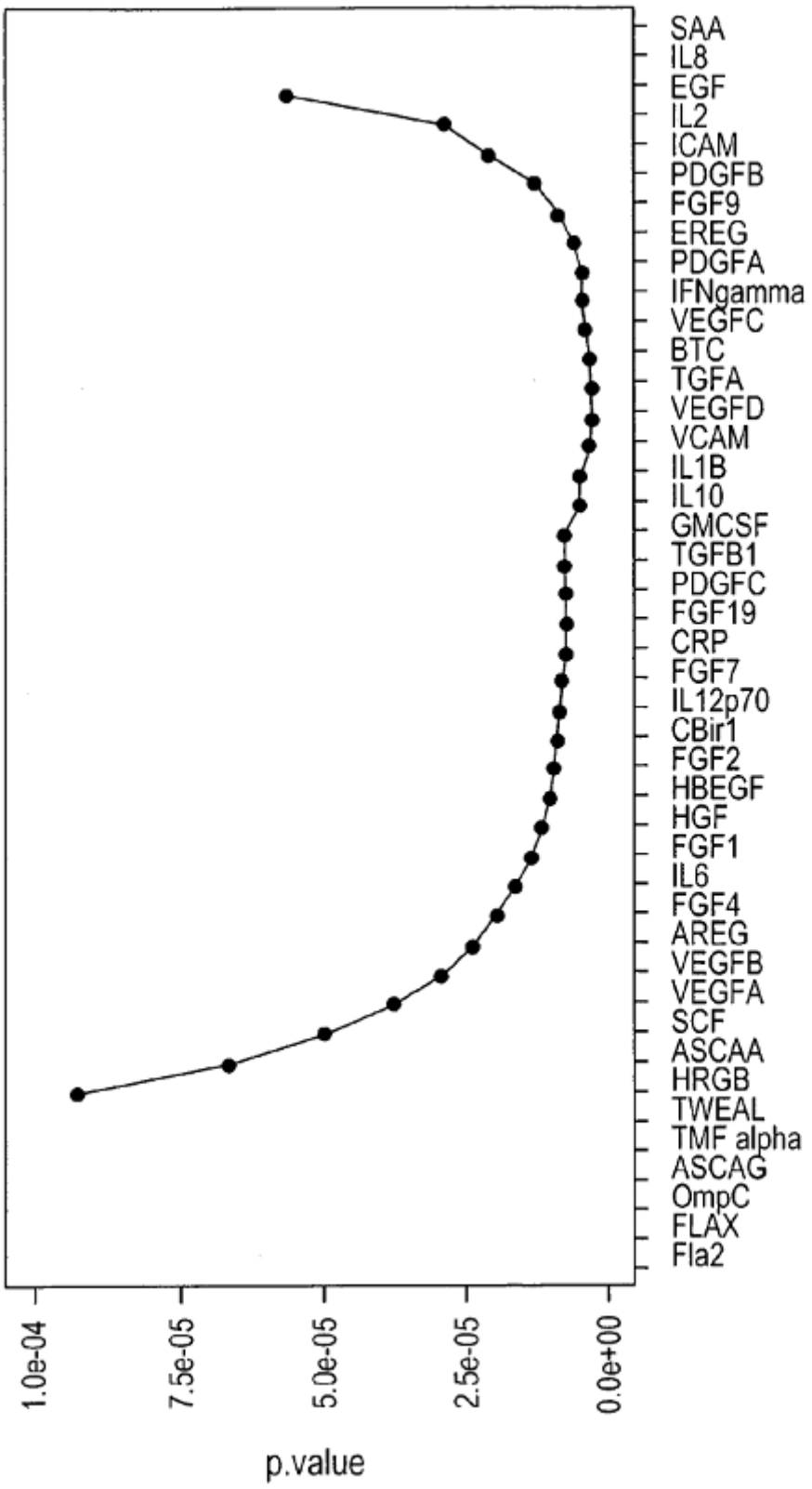

SAA
IL8
EGF
IL2
ICAM
PDGFB
FGF9
EREG
PDGFA
IFNgamma
VEGFC
BTC
TGFA
VEGFD
VCAM
IL1B
IL10
GMCSF
TGFB1
PDGFC
FGF19
CRP
FGF7
IL12p70
CBir1
FGF2
HBEGF
HGF
FGF1
IL6
FGF4
AREG
VEGFB
VEGFA
SCF
ASCAA
HRGB
TWEAL
TMF alpha
ASCAG
OmpC
FLAX
Fla2
MarkerCut
1.0e-04
7.5e-05
5.0e-05
2.5e-05
0.0e+00
p.value

FIG. 34C