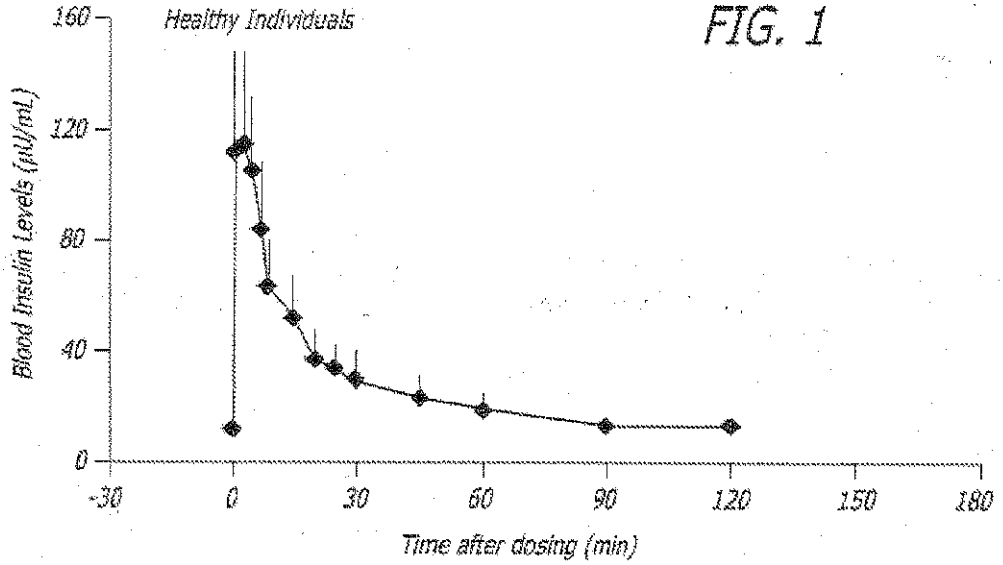

Healthy Individuals
Blood Insulin Levels (pU/mL)
160
120
80
40
0
-30
0
30
60
90
120
150
180
Time after dosing (min)

FIG. 1

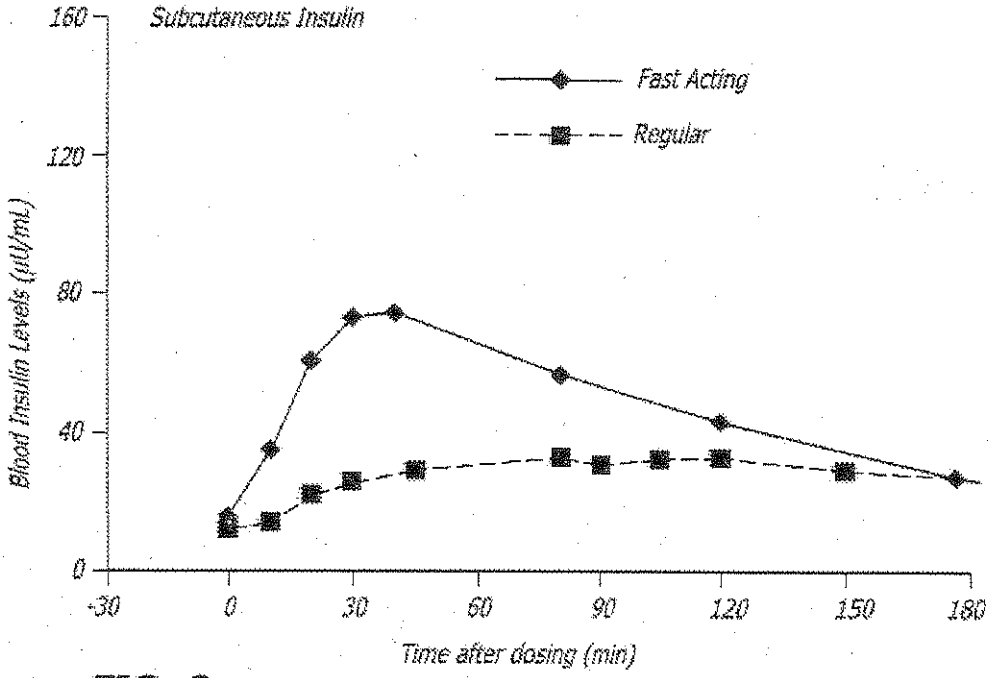

Subcutaneous Insulin
Fast Acting
Regular
Blood Insulin Levels (μU/mL)
160
120
80
40
0
-30
0
30
60
90
120
150
180
Time after dosing (min)

FIG. 2

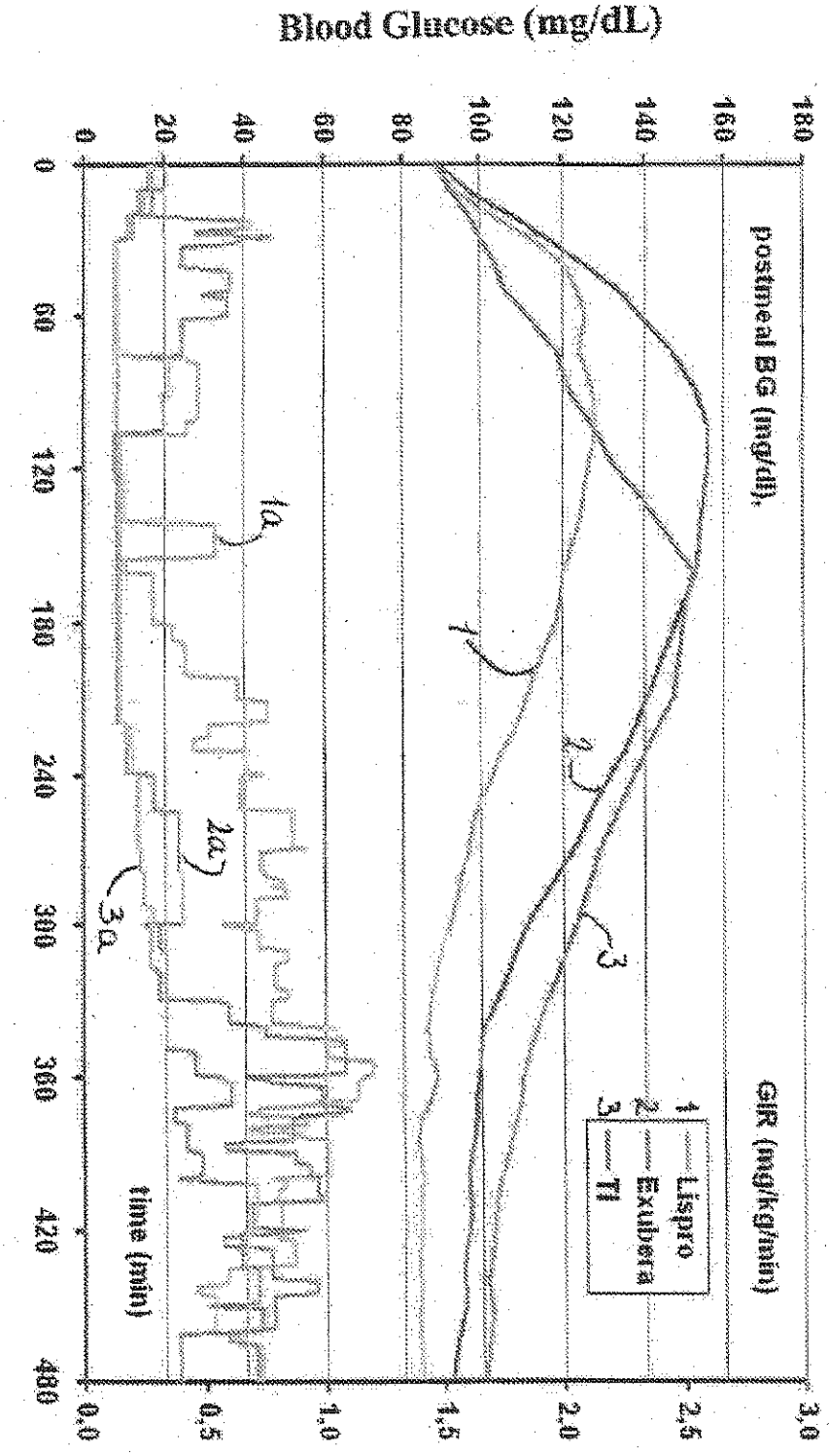

Blood Glucose (mg/dL)
postmeal BG (mg/dl),
GIR (mg/kg/min)
time (min)
Time (min)
Lispro
Exubera
TI
1
2
3
1a
2a
3a

FIG. 3

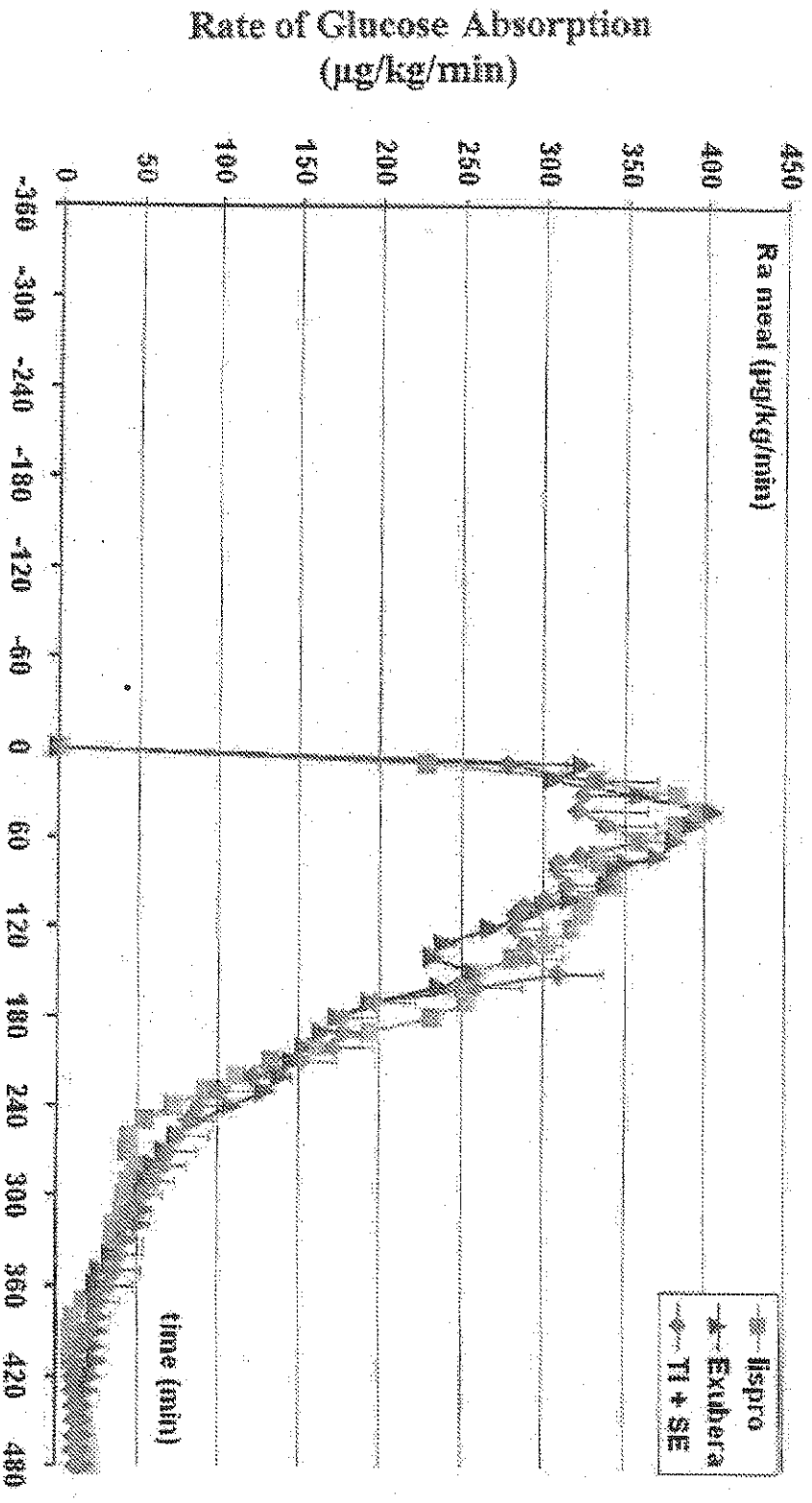
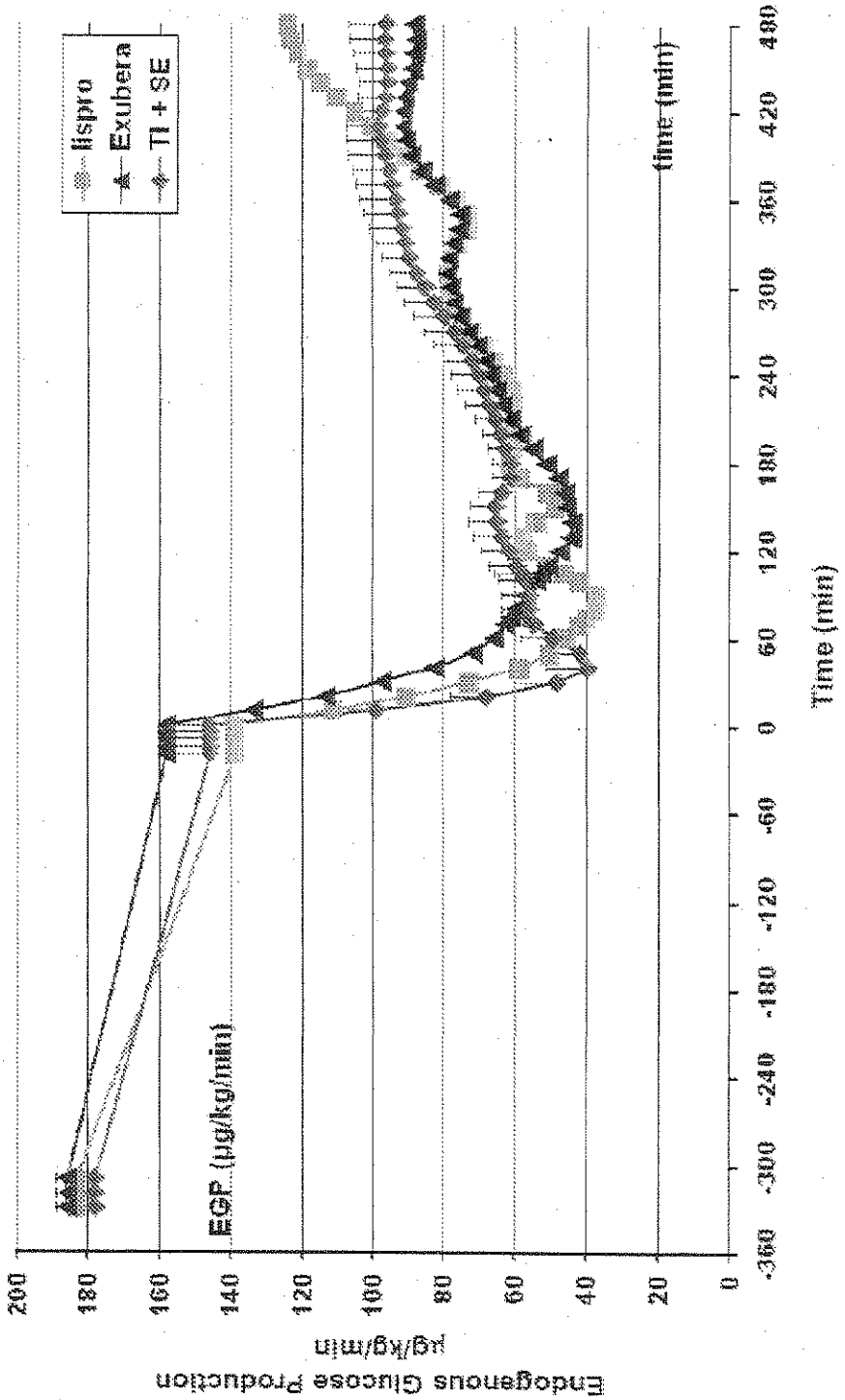

Rate of Glucose Absorption
(µg/kg/min)
Ra meal (µg/kg/min)
0
50
100
150
200
250
300
350
400
450
-360
-300
-240
-180
-120
-60
0
60
120
180
240
300
360
420
480
time (min)
Time (min)
Ilspro
Exubera
TI + SE

FIG. 4

Figure 5


Endogenous Glucose Production
µg/kg/min
200
180
160
140
120
100
80
60
40
20
0
-360
-300
-240
-180
-120
-60
0
60
120
180
240
300
360
420
480
Time (min)
time (min)
EGP (µg/kg/min)
lispro
Exubera
TI + SE

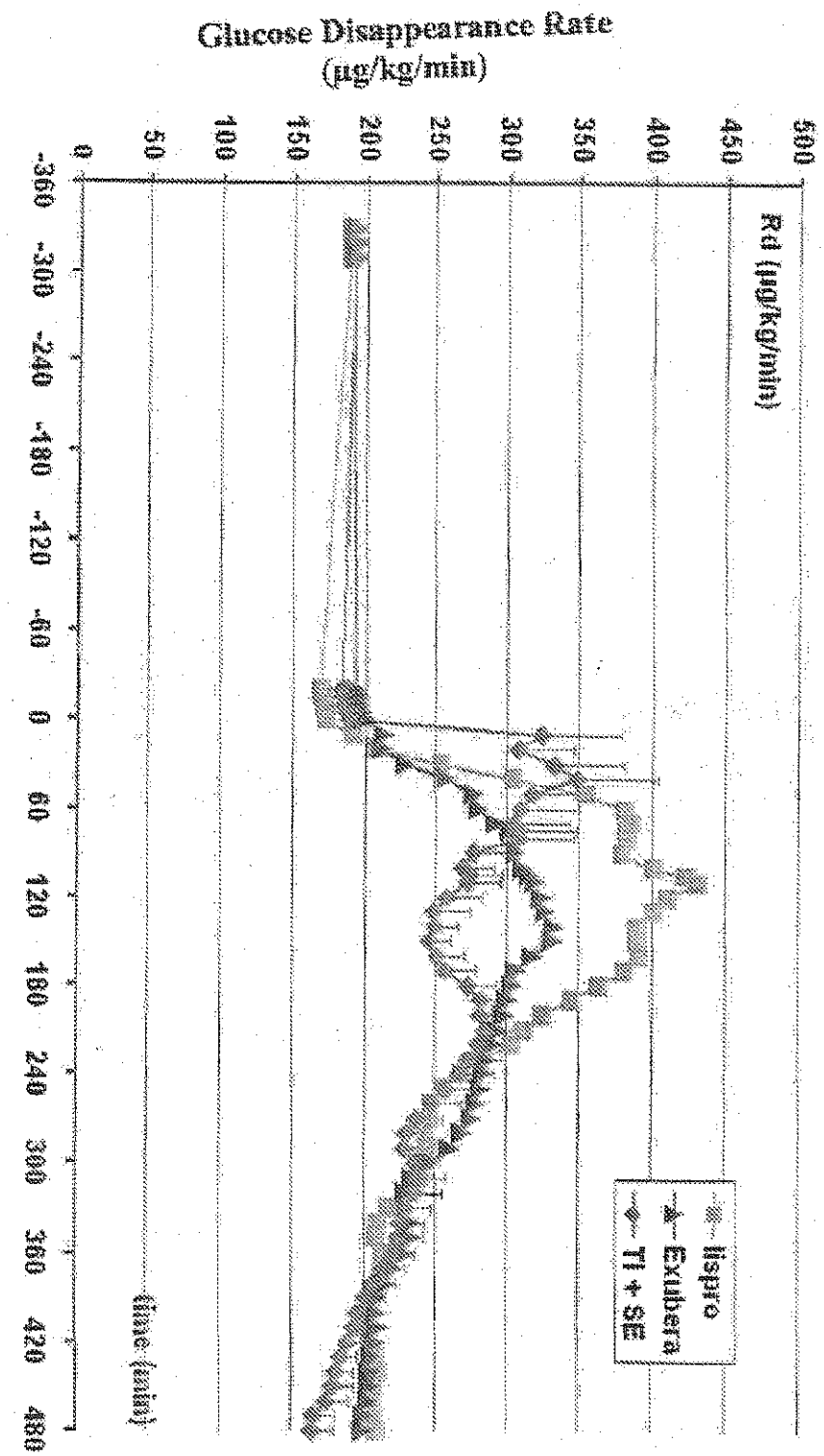

Glucose Disappearance Rate
(µg/kg/min)
Rd (µg/kg/min)
500
450
400
350
300
250
200
150
100
50
0
-360
-300
-240
-180
-120
-60
0
60
120
180
240
300
360
420
480
time (min)
Time (min)
Lispro
Exubera
TI + SE

FIG. 6

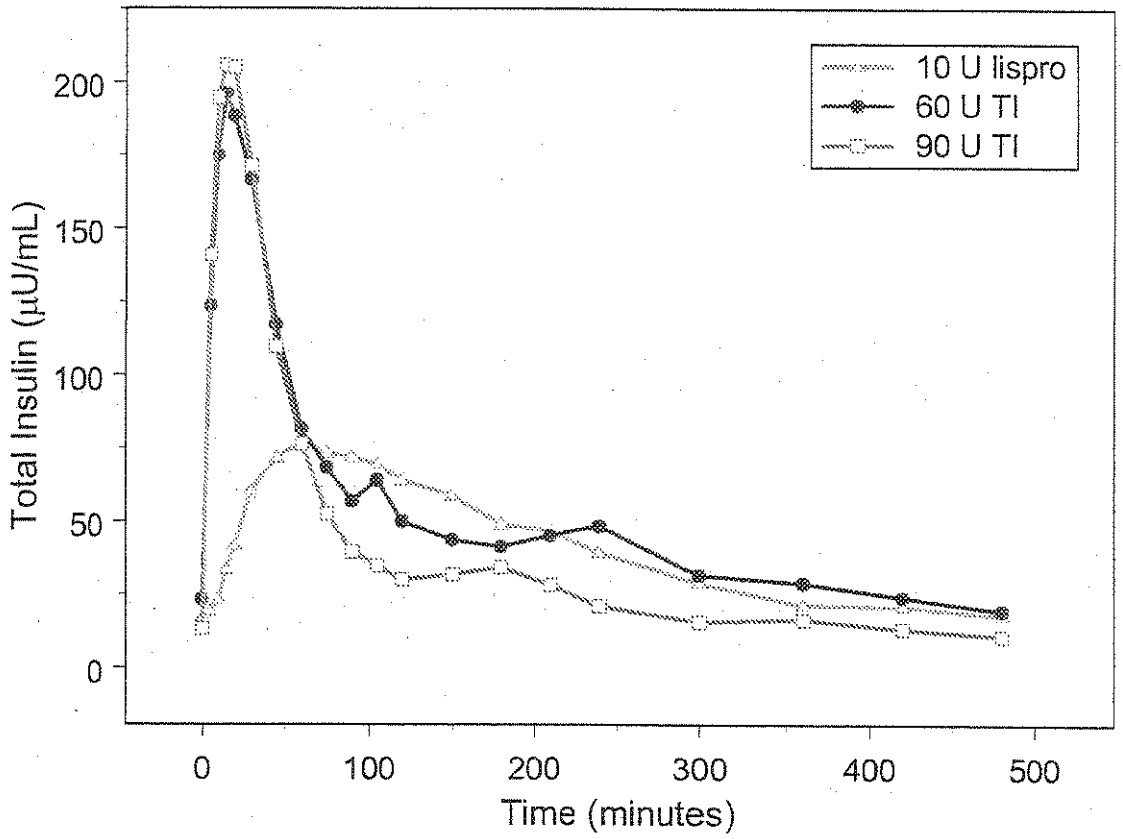

10 U lispro
60 U TI
90 U TI
Total Insulin (µU/mL)
200
150
100
50
0
0
100
200
300
400
500
Time (minutes)

FIG. 7

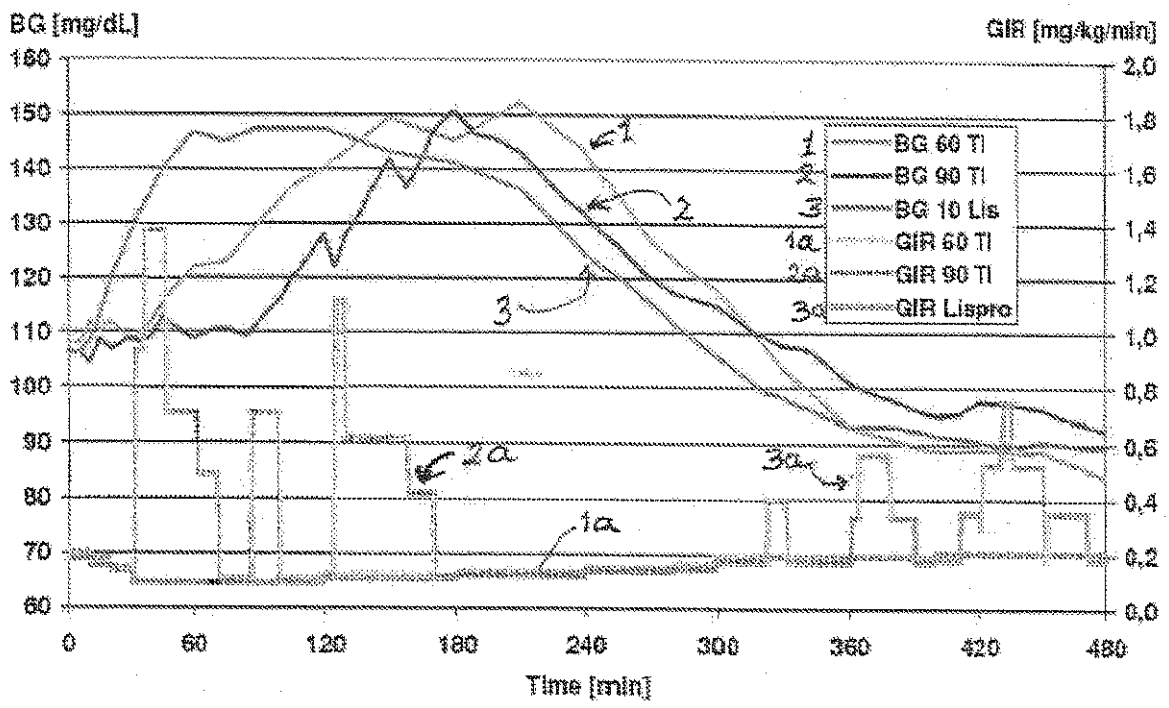

BG [mg/dL]
GIR [mg/kg/min]
160
150
140
130
120
110
100
90
80
70
60
2,0
1,8
1,6
1,4
1,2
1,0
0,8
0,6
0,4
0,2
0,0
0
60
120
180
240
300
360
420
480
Time [min]
1
2
3
1a
2a
3a
BG 60 TI
BG 90 TI
BG 10 Lis
GIR 60 TI
GIR 90 TI
GIR Lispro

FIG. 8

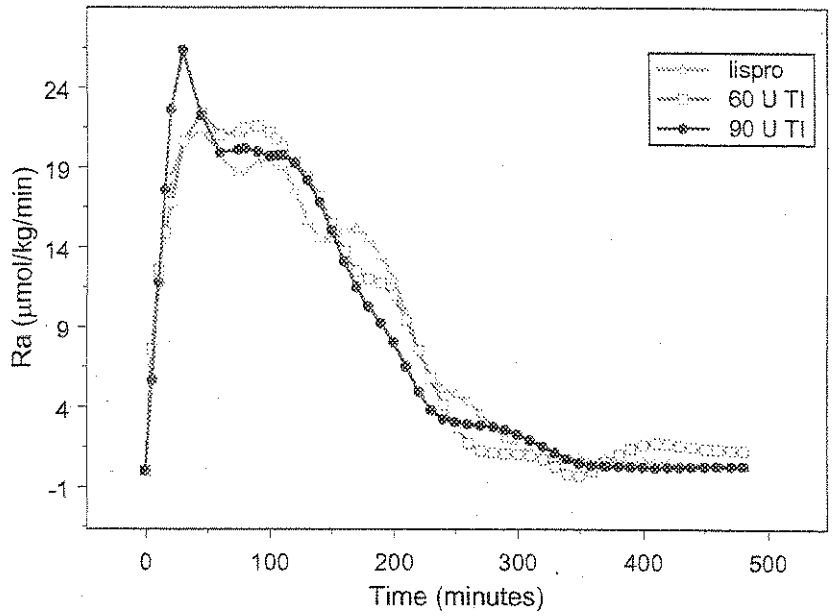

lispro
60 U TI
90 U TI
Ra (µmol/kg/min)
24
19
14
9
4
-1
0
100
200
300
400
500
Time (minutes)

FIG. 9

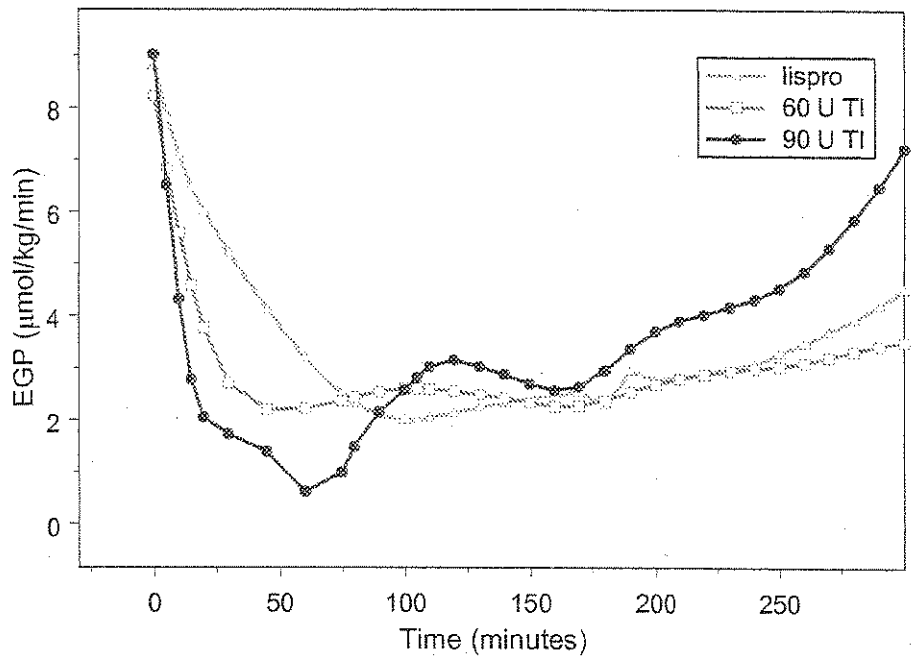

lispro
60 U TI
90 U TI
EGP (µmol/kg/min)
8
6
4
2
0
0
50
100
150
200
250
Time (minutes)

FIG. 10

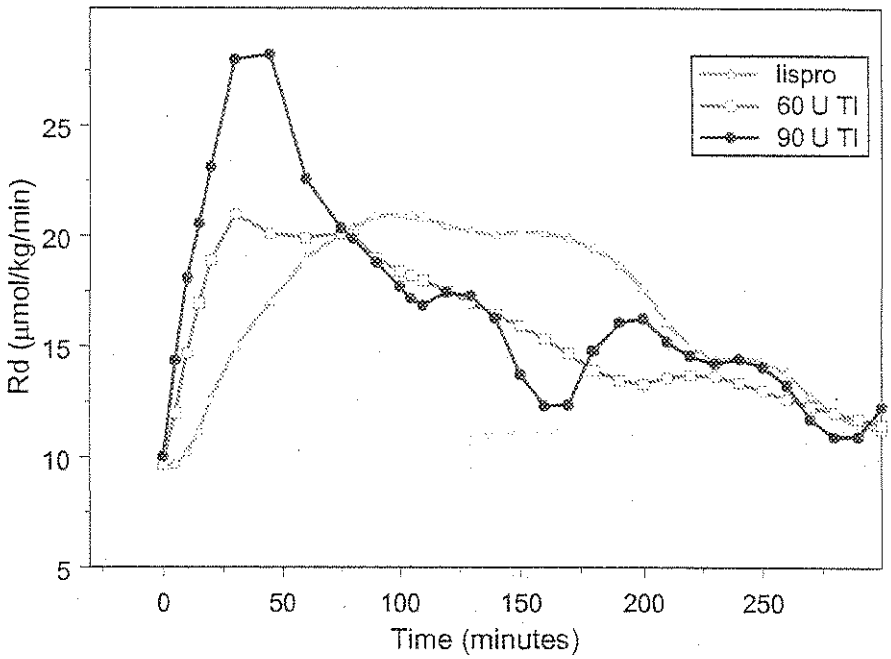

lispro
60 U TI
90 U TI
Rd (µmol/kg/min)
25
20
15
10
5
0
50
100
150
200
250
Time (minutes)

FIG. 11

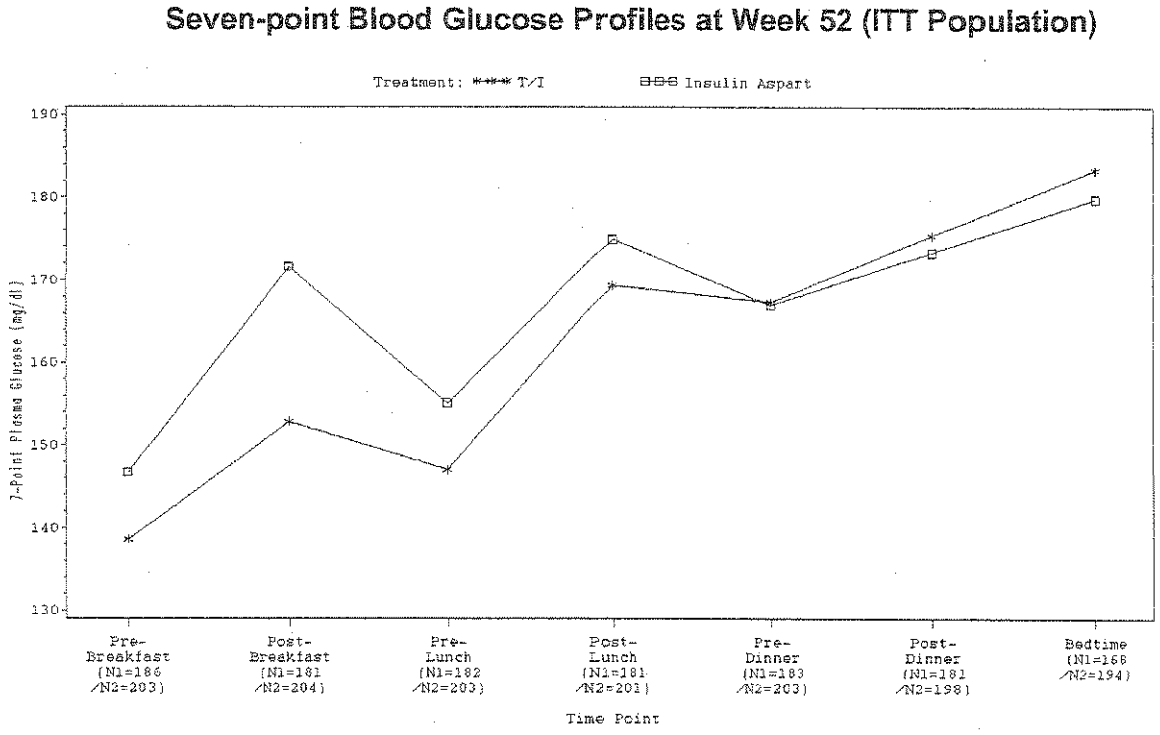

Seven-point Blood Glucose Profiles at Week 52 (ITT Population)
Treatment: T/I
Insulin Aspart
7-Point Plasma Glucose (mg/dl)
190
180
170
160
150
140
130
Pre-Breakfast (N1=186 /N2=203)
Post-Breakfast (N1=181 /N2=204)
Pre-Lunch (N1=182 /N2=203)
Post-Lunch (N1=181 /N2=201)
Pre-Dinner (N1=183 /N2=203)
Post-Dinner (N1=181 /N2=198)
Bedtime (N1=168 /N2=194)
Time Point

FIG. 12

FIG. 13

Fasting blood glucose over time.

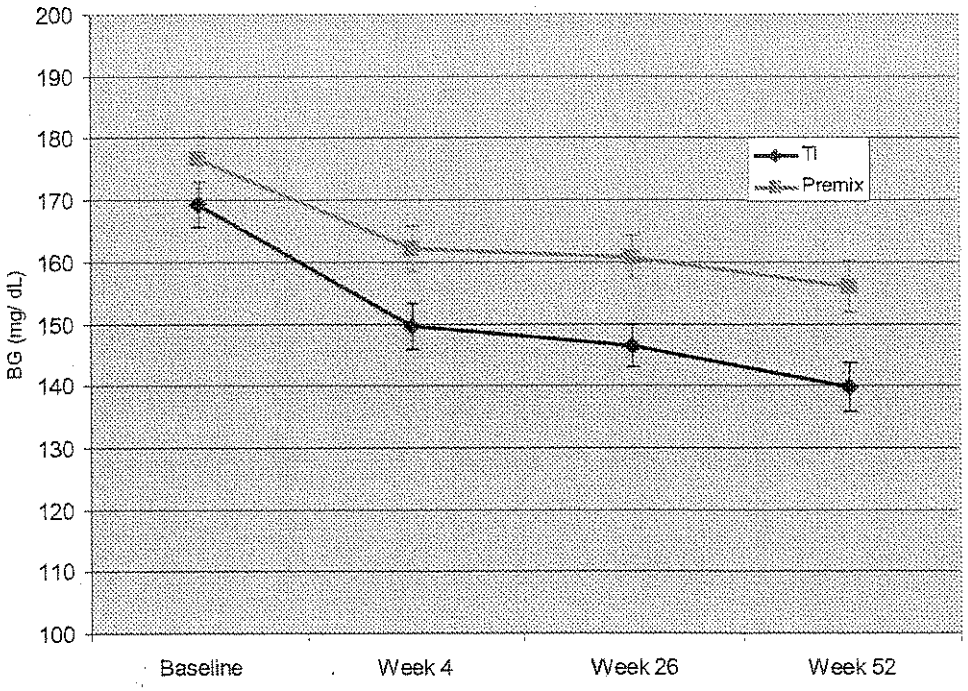
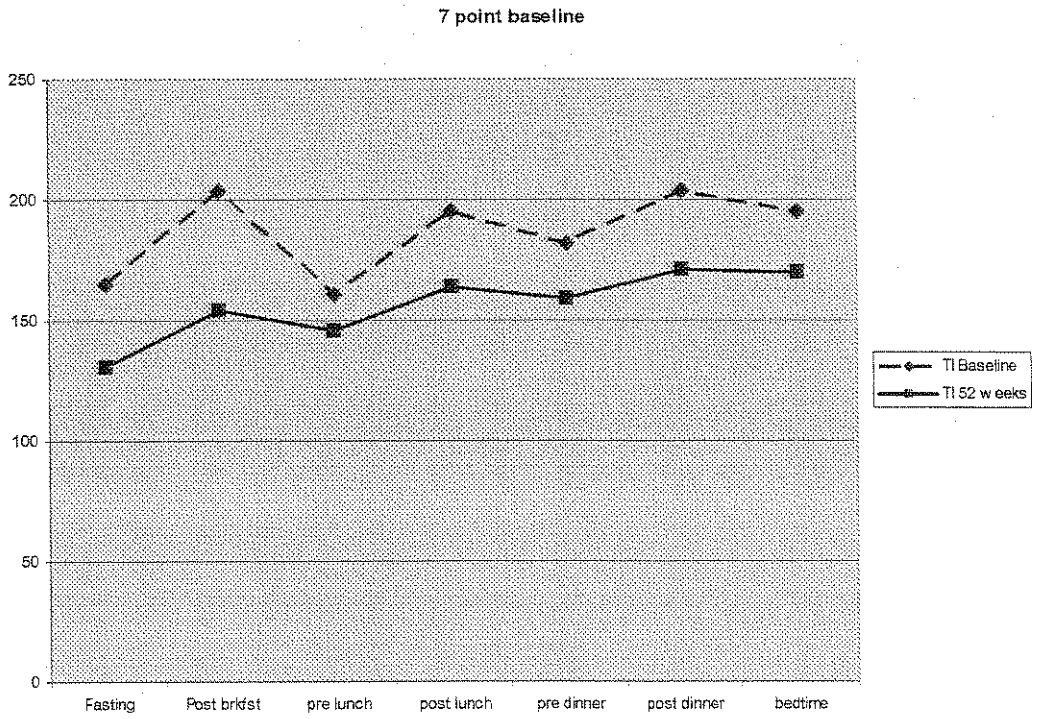


FIG. 14

Seven point blood glucose profile: baseline and 52 weeks.



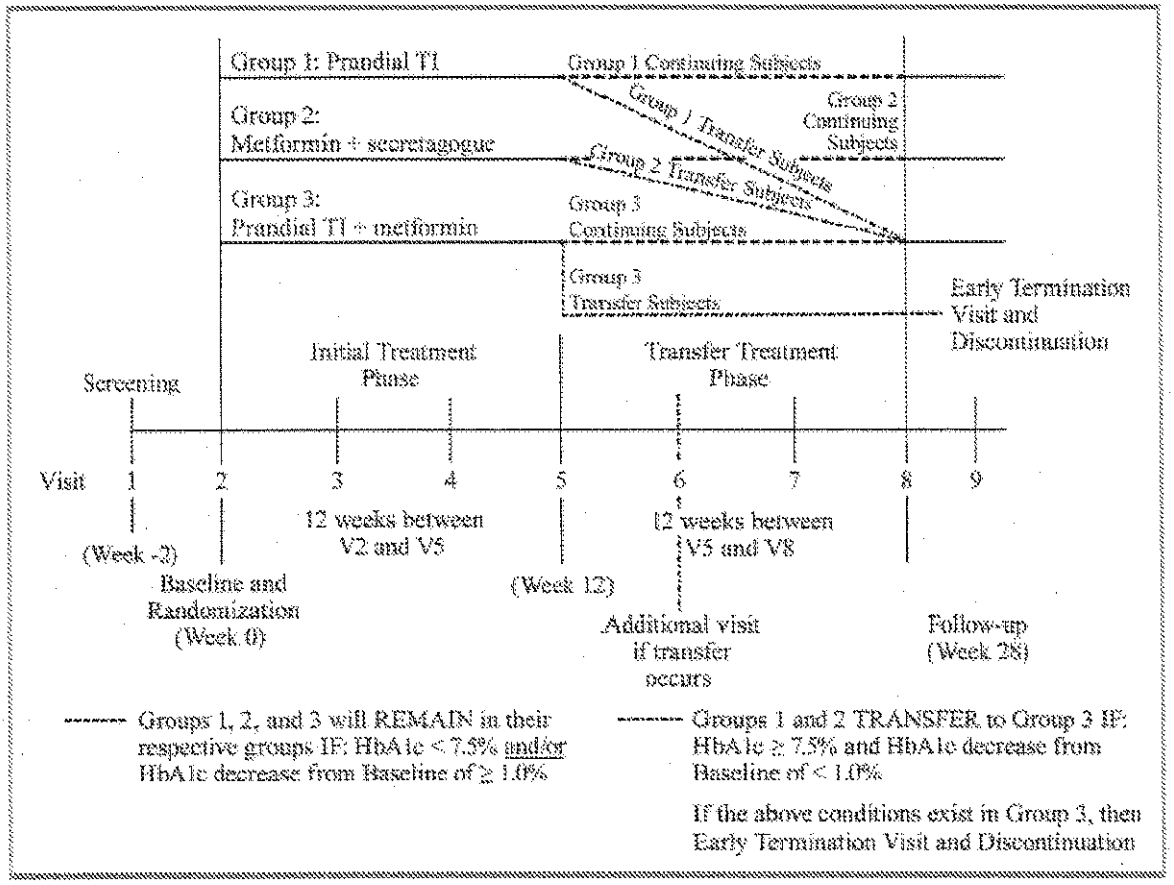
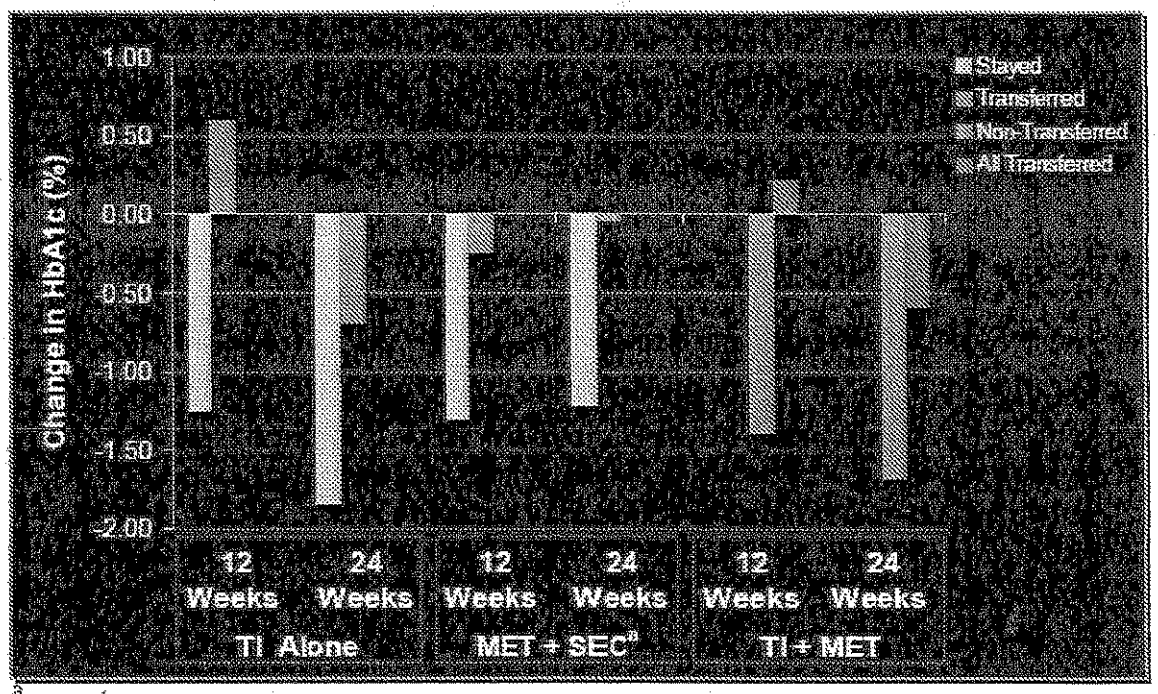

Group 1: Prandial TI
Group 1 Continuing Subjects
Group 1 Transfer Subjects
Group 2
Continuing
Subjects
Group 2:
Metformin + secretagogue
Group 2 Transfer Subjects
Group 3:
Prandial TI + metformin
Group 3
Continuing Subjects
Group 3
Transfer Subjects
Early Termination
Visit and
Discontinuation
Initial Treatment
Phase
Transfer Treatment
Phase
Screening
Visit 1 2 3 4 5 6 7 8 9
12 weeks between
V2 and V5
12 weeks between
V5 and V8
(Week -2)
Baseline and
Randomization
(Week 0)
(Week 12)
Additional visit
if transfer
occurs
Follow-up
(Week 28)
Groups 1, 2, and 3 will REMAIN in their respective groups IF: HbA1c < 7.5% and/or HbA1c decrease from Baseline of ≥ 1.0%
Groups 1 and 2 TRANSFER to Group 3 IF: HbA1c ≥ 7.5% and HbA1c decrease from Baseline of < 1.0%
If the above conditions exist in Group 3, then Early Termination Visit and Discontinuation

FIG. 15

FIG. 16

Demographic and Baseline Characteristics by Randomized Treatment Group (ITT Population)				
Characteristic	Statistic	TI Alone (n = 177)	Metformin + Secretagogue (n = 162)	TI + Metformin (n = 169)
Gender, Number of Subjects (%)				
➢ Male		84 (47.5)	74 (45.7)	68 (40.2)
➢ Female		93 (52.5)	88 (54.3)	101 (59.8)
Race, Number of Subjects (%)				
➢ Caucasian		133 (75.1)	114 (70.4)	129 (76.3)
➢ Black		9 (5.1)	8 (4.9)	12 (7.1)
➢ Asian		4 (2.3)	5 (3.1)	2 (1.2)
➢ Hispanic		26 (14.7)	25 (15.4)	23 (13.6)
➢ Other		5 (2.8)	10 (6.2)	3 (1.8)
Age, Years				
	Mean (SD)	57.3 (8.47)	57.6 (9.14)	56.8 (8.31)
Weight, Kilograms				
	Mean (SD)	86.14 (15.59)	84.18 (16.21)	83.87 (13.93)
BMI, kg/m2				
	Mean (SD)	31.23 (4.30)	30.73 (4.61)	30.81 (4.40)
Baseline HbA1c (%)				
	Mean (SD)	8.92 (0.96)	8.90 (0.94)	8.95 (0.97)
Fasting Plasma Glucose (mg/dL)				
	Mean (SD)	193.59 (53.68)	197.31 (47.96)	189.39 (47.34)

* Percentages are based on the number of subjects in each treatment group in the specified population (n). Statistics are summarized by the randomized treatment group. SD=Standard Deviation



[a] secretagogue

FIG. 17

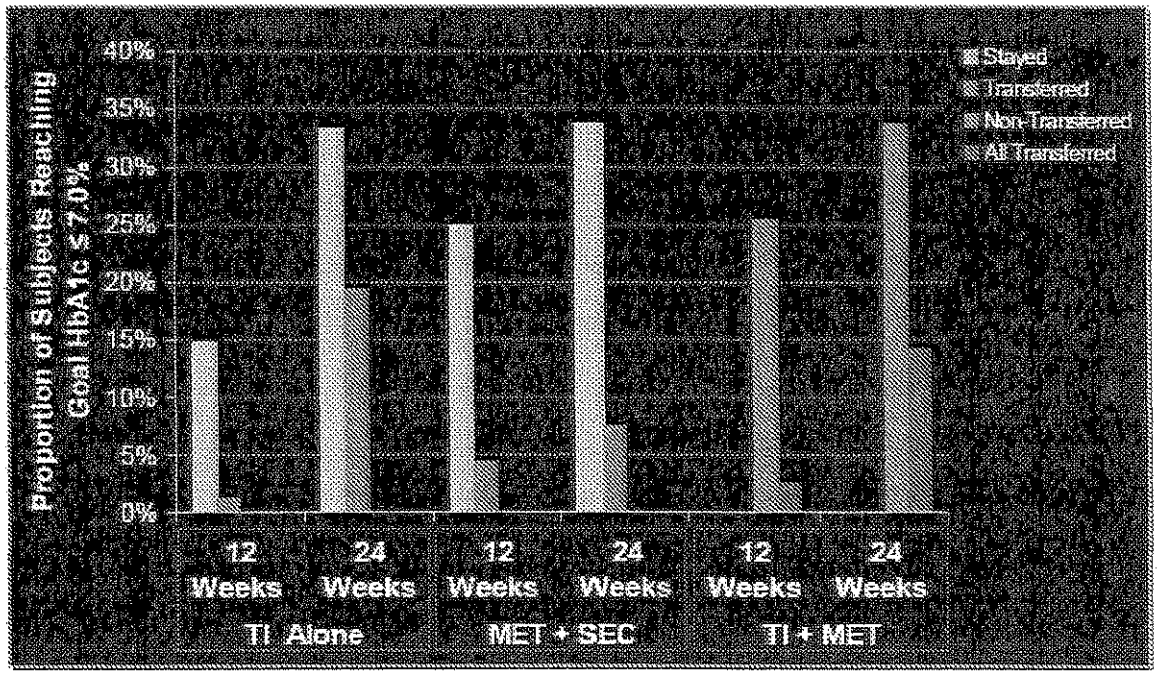


FIG. 18

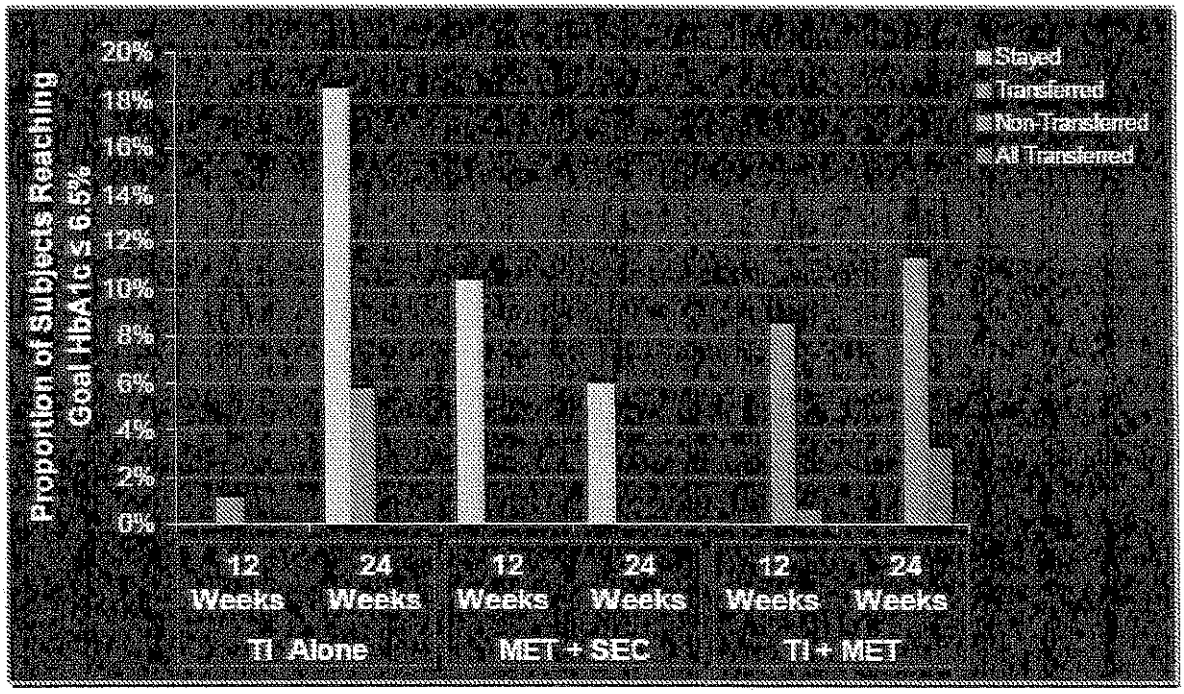

Proportion of Subjects Reaching Goal HbA1c ≤ 6.5%
20%
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
Stayed
Transferred
Non-Transferred
All Transferred
12 Weeks
24 Weeks
12 Weeks
24 Weeks
12 Weeks
24 Weeks
TI Alone
MET + SEC
TI + MET

FIG. 19

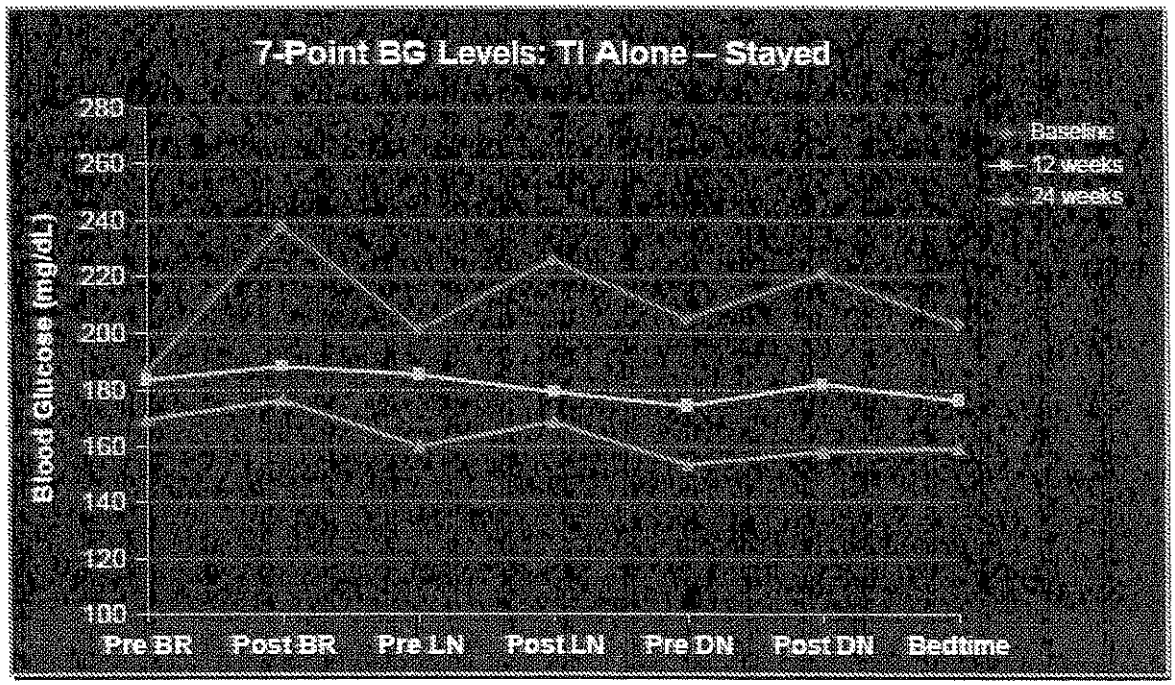

7-Point BG Levels: TI Alone – Stayed
Blood Glucose (mg/dL)
280
260
240
220
200
180
160
140
120
100
Baseline
12 weeks
24 weeks
Pre BR
Post BR
Pre LN
Post LN
Pre DN
Post DN
Bedtime

FIG. 20

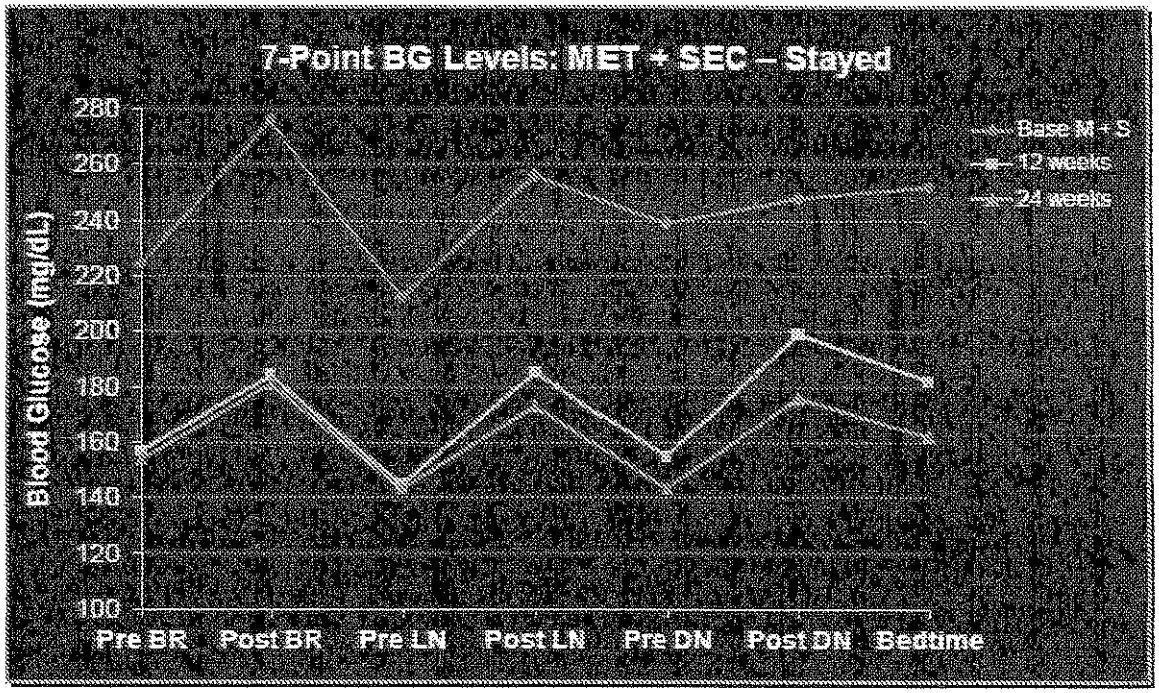

7-Point BG Levels: MET + SEC – Stayed
Blood Glucose (mg/dL)
280
260
240
220
200
180
160
140
120
100
Pre BR
Post BR
Pre LN
Post LN
Pre DN
Post DN
Bedtime
Base M + S
12 weeks
24 weeks

FIG. 21

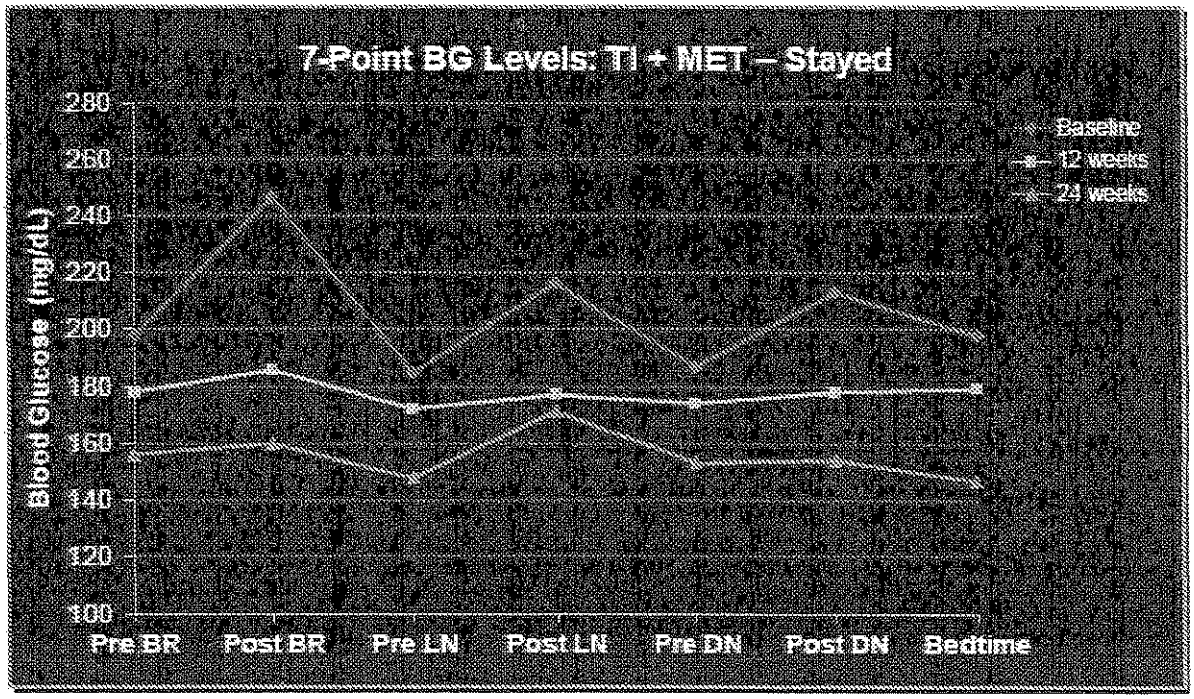

7-Point BG Levels: TI + MET – Stayed
Blood Glucose (mg/dL)
280
260
240
220
200
180
160
140
120
100
Pre BR
Post BR
Pre LN
Post LN
Pre DN
Post DN
Bedtime
Baseline
12 weeks
24 weeks

FIG. 22

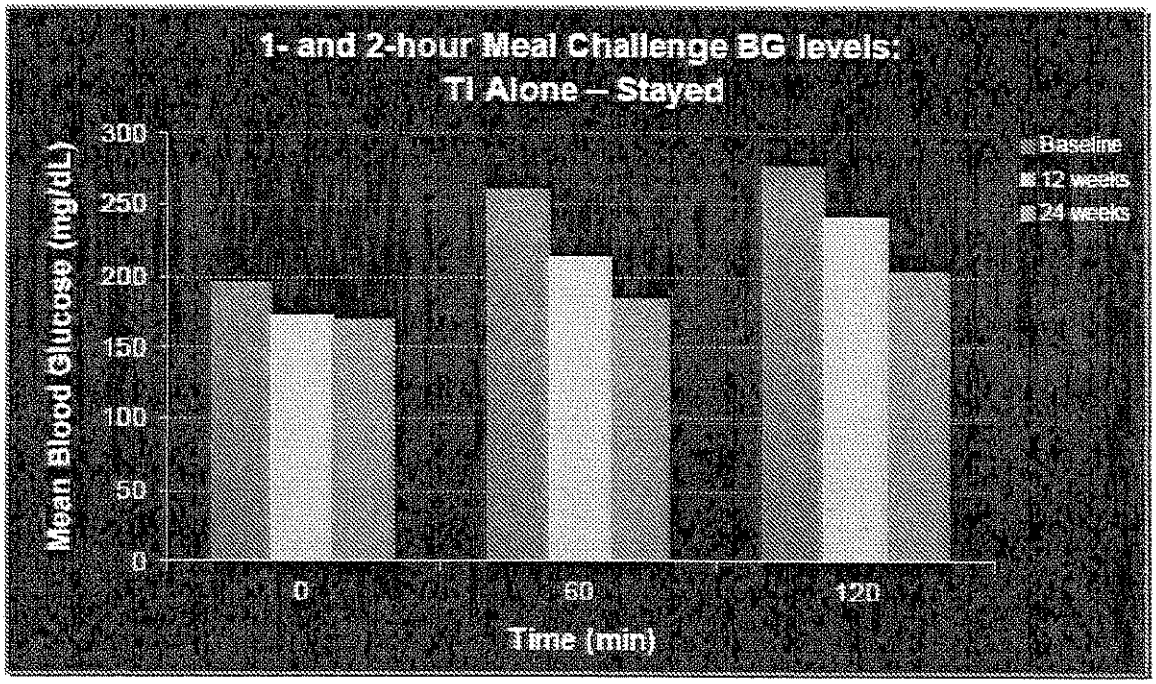

1- and 2-hour Meal Challenge BG levels:
TI Alone – Stayed
Mean Blood Glucose (mg/dL)
300
250
200
150
100
50
0
0
60
120
Time (min)
Baseline
12 weeks
24 weeks

FIG. 23

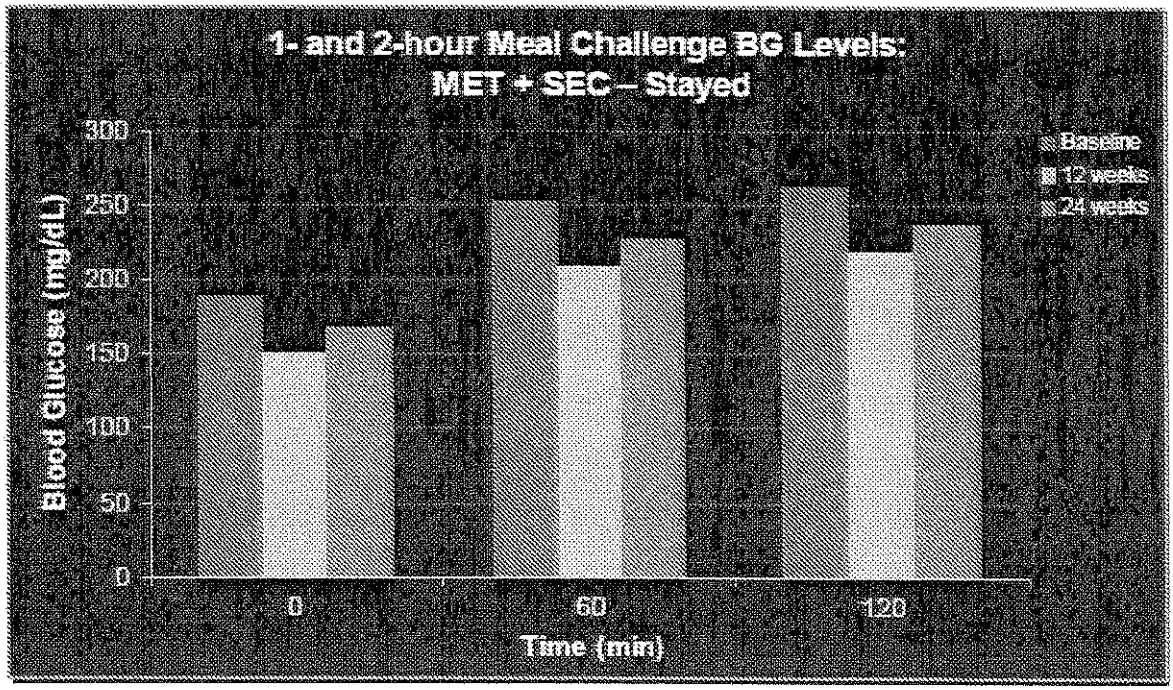

1- and 2-hour Meal Challenge BG Levels:
MET + SEC – Stayed
Blood Glucose (mg/dL)
300
250
200
150
100
50
0
0
60
120
Time (min)
Baseline
12 weeks
24 weeks

FIG. 24

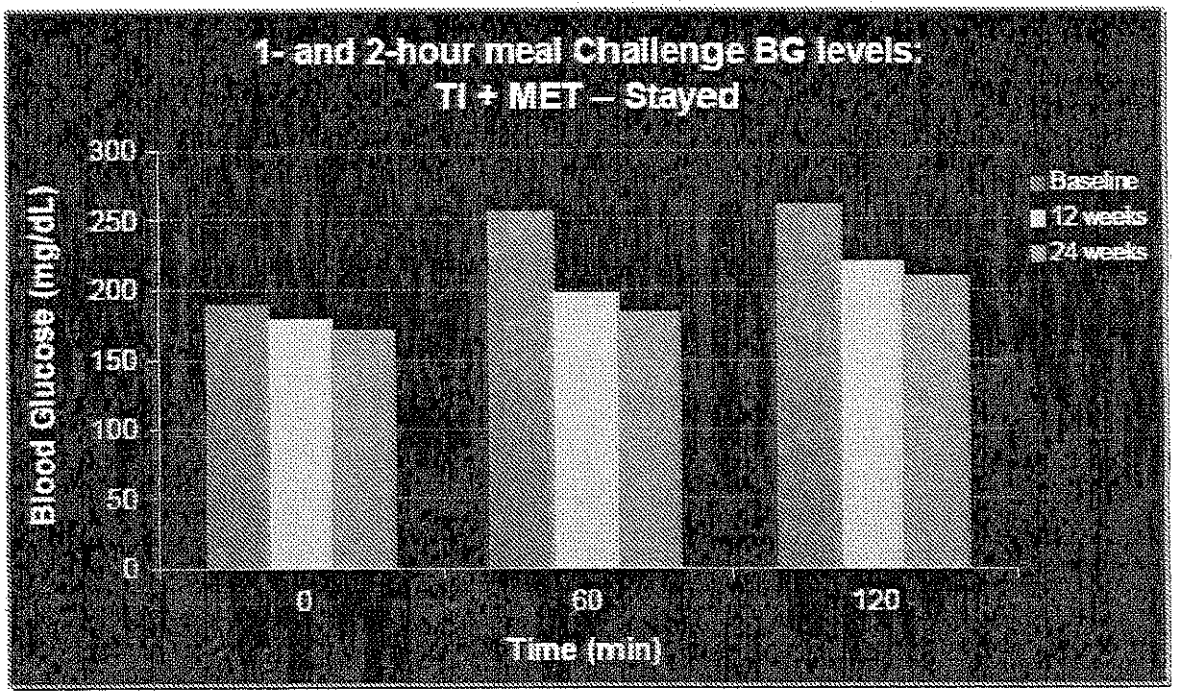

1- and 2-hour meal Challenge BG levels:
TI + MET – Stayed
Blood Glucose (mg/dL)
300
250
200
150
100
50
0
0
60
120
Time (min)
Baseline
12 weeks
24 weeks

FIG. 25

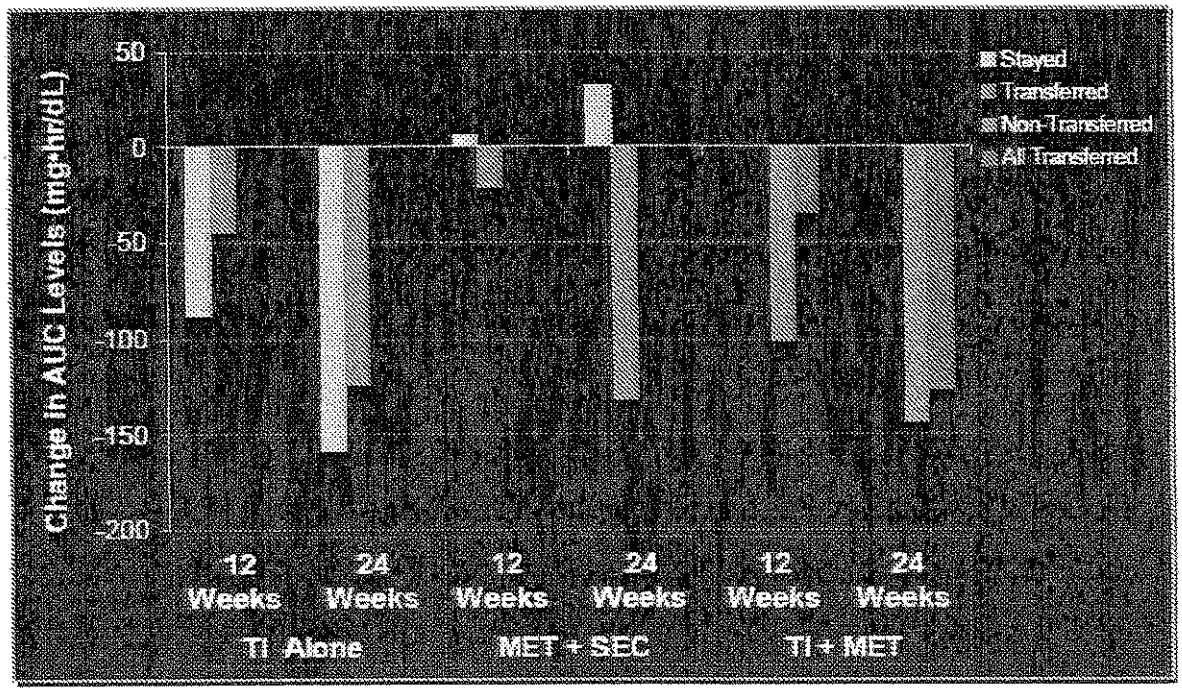

Change in AUC Levels (mg-hr/dL)
50
0
-50
-100
-150
-200
Stayed
Transferred
Non-Transferred
All Transferred
12 Weeks
24 Weeks
12 Weeks
24 Weeks
12 Weeks
24 Weeks
TI Alone
MET + SEC
TI + MET

FIG. 26

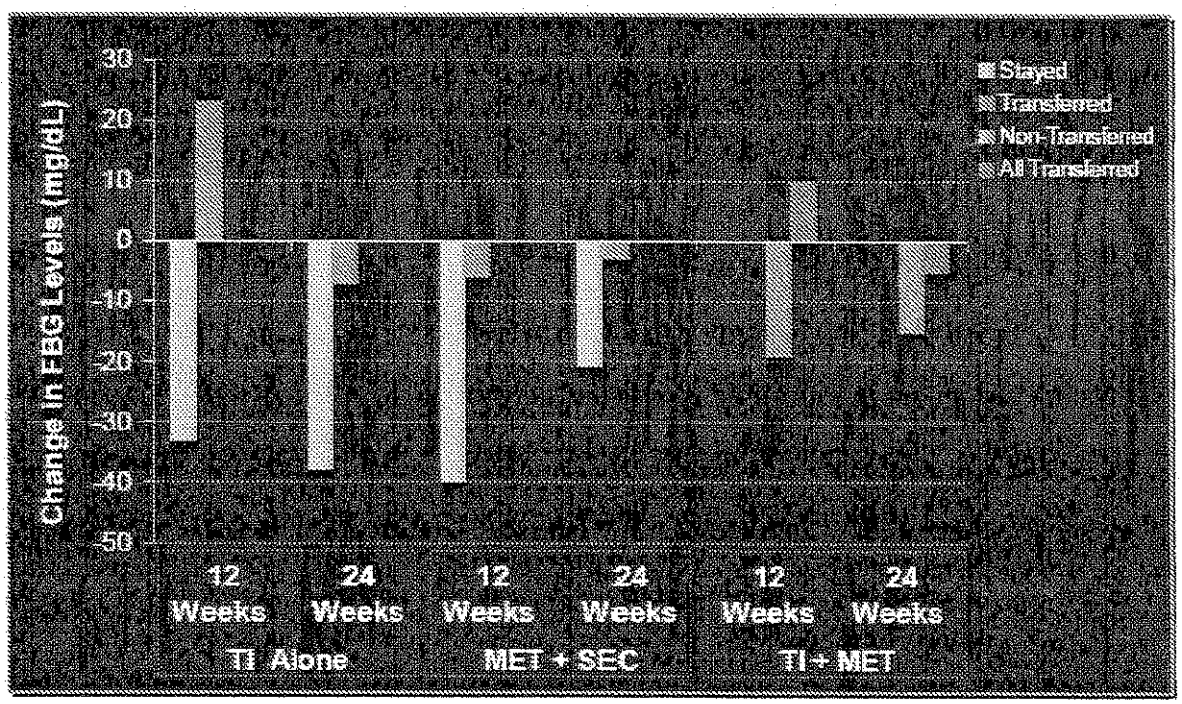

Change in FBG Levels (mg/dL)
30
20
10
0
-10
-20
-30
-40
-50
Stayed
Transferred
Non-Transferred
All Transferred
12 Weeks
24 Weeks
12 Weeks
24 Weeks
12 Weeks
24 Weeks
TI Alone
MET + SEC
TI + MET

FIG. 27

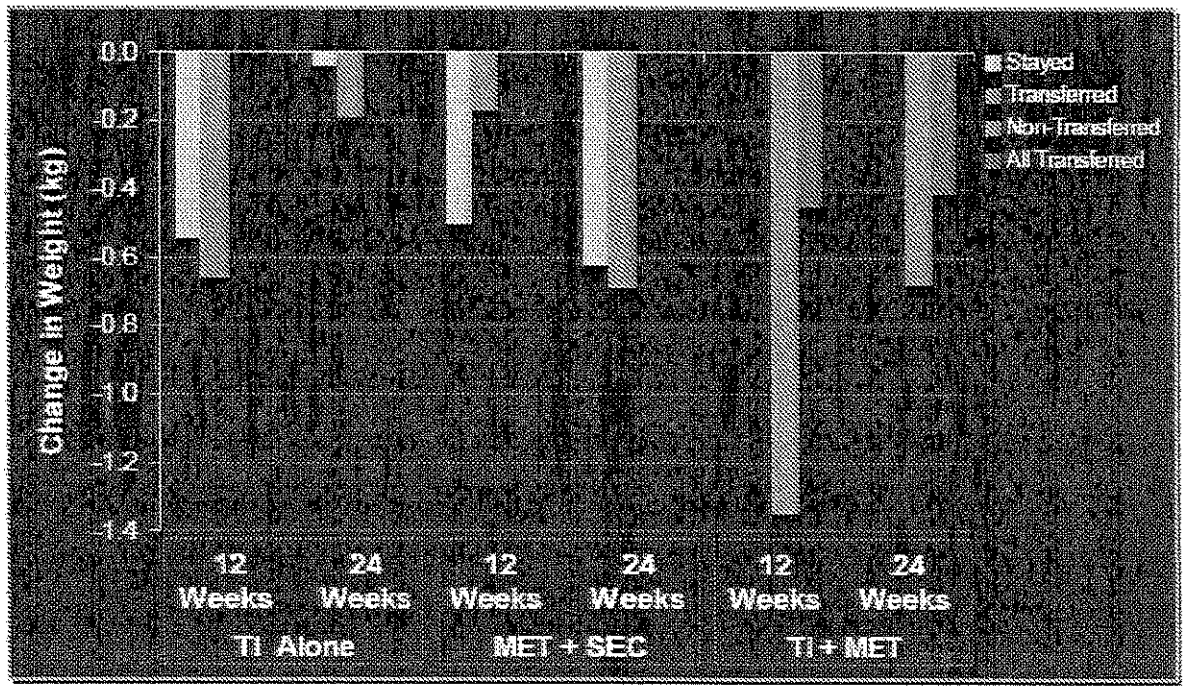

Change in Weight (kg)
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
-1.2
-1.4
Stayed
Transferred
Non-Transferred
All Transferred
12 Weeks
24 Weeks
12 Weeks
24 Weeks
12 Weeks
24 Weeks
TI Alone
MET + SEC
TI + MET

FIG. 28